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1997–98 Influenza Summary

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The 1997–98 influenza season began in mid-November. On November 18, 1997, two, symptomatic 3-year-old children were cultured for influenza by the Cape Girardeau County Public Health Center. The cultures were sent to the State Public Health Laboratory and then the influenza isolates were forwarded to the Centers for Disease Control and Prevention (CDC). The two specimens were the first Missouri laboratory-confirmed cases of influenza A/Wuhan/395/95-like (H3N2) for the 1997–98 season.

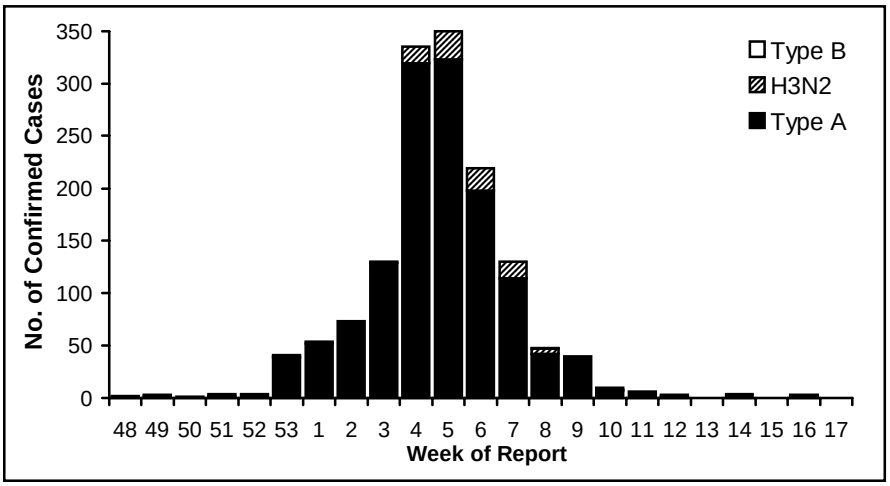

Figure 1. Laboratory-confirmed influenza cases by week of report, Missouri, 1997–98 season.

There was a total of 1,462 laboratory-confirmed cases of influenza reported in Missouri during the 1997–98 season. Of the 1,462 confirmed cases, 1,459 (99.8%) were type A, with 99 subtyped as H3N2. There were three (0.2%) confirmed cases of type B influenza reported in Missouri. Confirmed influenza type A cases peaked during week 5. See Figure 1.

During January and February, the Department of Health received ten reports of influenza-like illness outbreaks in long-term care facilities. Another influenza-like outbreak occurred in March. Four of the outbreaks were confirmed as type A, but none of the specimens were subtyped.

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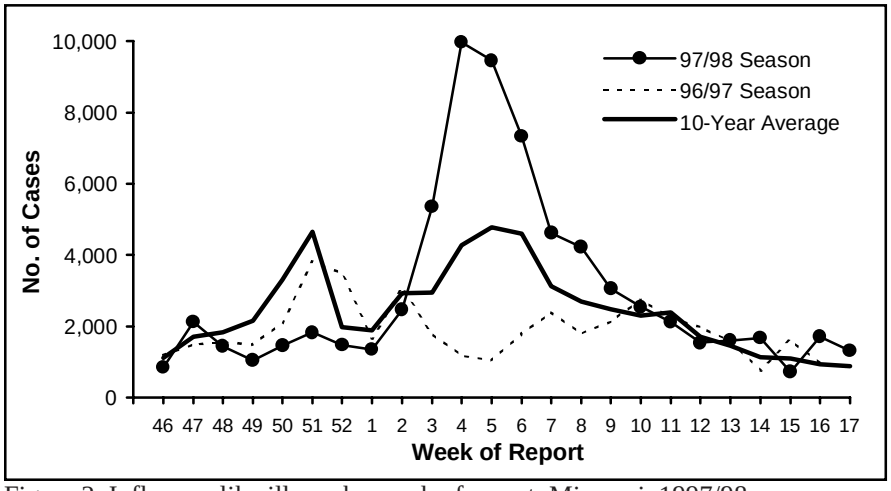

Figure 2. Influenza-like illness by week of report, Missouri, 1997/98 season, 1996/97 season and 1987–97 average.

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Most notable during this influenza season were the large number of schools and school districts that cancelled classes from one to four days due to influenza-like illness absenteeism. From mid-January to mid-February, 29 schools reported increased student, teacher and staff absenteeism due to influenza-like illness. During the same period, three communities, three correctional facilities and one university reported influenza-like illness outbreaks. One community, two correctional facilities and the university submitted culture specimens related to the outbreaks to the State Public Health Laboratory that confirmed influenza A, subtype H3N2.

Confirmed cases of influenza type A began increasing during week 53 and peaked during week 5. The established Missouri active surveillance sites reporting to local health agencies and Missouri physicians participating in the U.S. Influenza Sentinel Physician Surveillance Network (see article on page 37) submitted data showing a rise of influenza-like illness starting in week 2 that peaked during week 4. Levels of confirmed influenza type A and reports of influenza-like illness gradually returned to baseline levels by week 10. See Figures 1 and 2.

The number of pneumonia and influenza deaths rose above the previous 10-year average during week 1 through week 13, and peaked during week 9. Additional peaks above the previous 10-year average also occurred during weeks 47, 49, 50, 51 and 16. See Figure 3.

Figure 4 shows laboratory-confirmed influenza cases by county of residence.

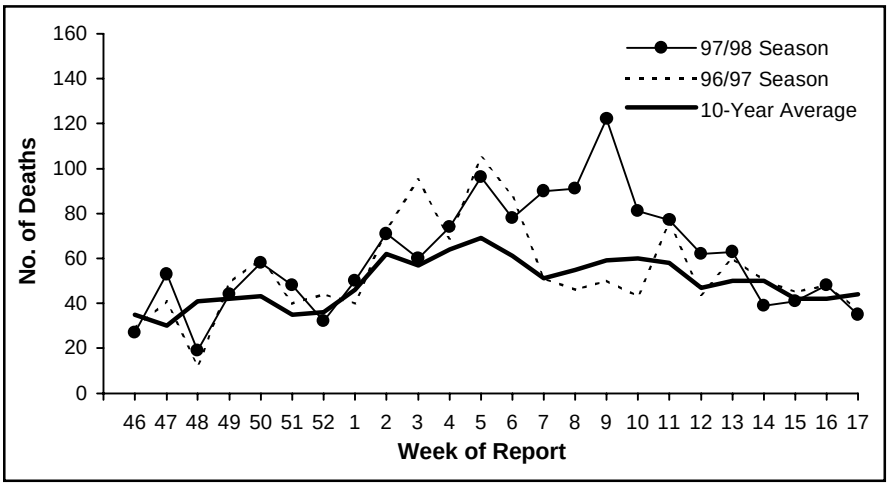

Figure 3. Pneumonia and influenza deaths by week of report, Missouri, 1997/98 season, 1996/97 season and 1987–97 average.

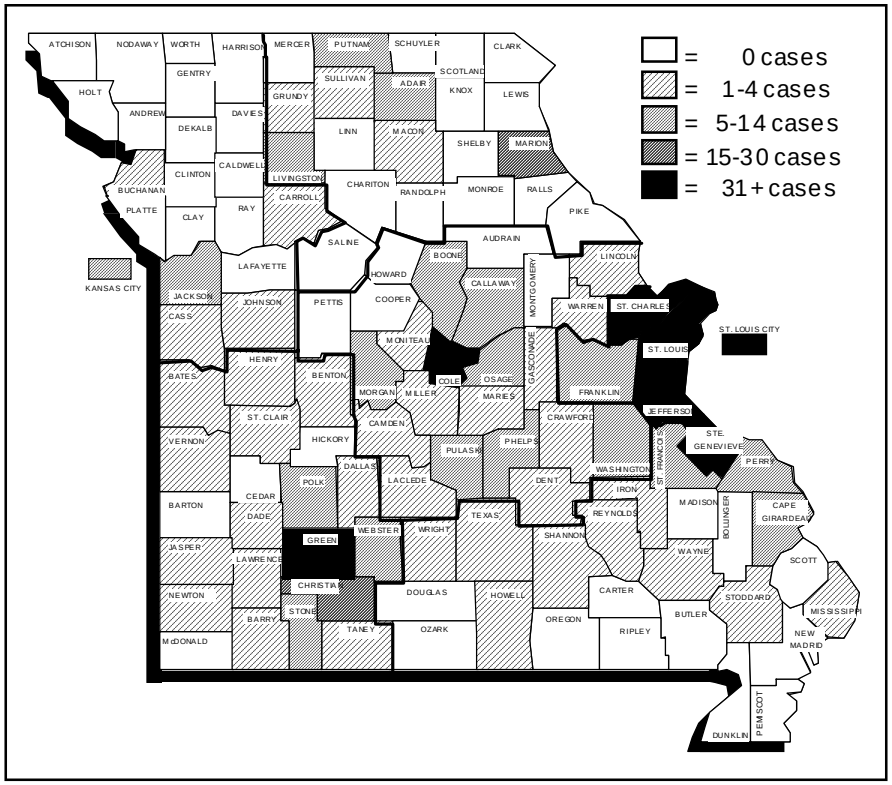

Figure 4. Laboratory-confirmed influenza cases by county of residence, Missouri, 1997–98 season.

During the 1997–98 influenza season, CDC performed antigenic characterization of influenza viruses. Of the 366 specimens submitted to their laboratory from various state health departments and antigenically characterized as influenza type A(H3N2), 16 percent were similar to A/Nanchang/933/95(H3N2), the A/Wuhan/359/95(H3N2)-like component of the 1997–98 influenza vaccine, and 84 percent were similar to A/Sydney/05/97(H3N2), a related but antigenically distinguishable variant of the A(H3N2) component of the 1997–98 influenza vaccine. CDC did confirm A/Sydney/05/97 (H3N2) virus in specimens submitted by the Missouri State Public Health Laboratory.

Influenza vaccine recommendations for 1998–99 can be found on pages 38–39 of this issue.

NOTE: Figures 2 and 3 do not include week 53 for comparison as week 53 does not occur in every influenza season. During week 53 of the 1997–98 season, 1,112 cases of influenza-like illness were reported through the active surveillance system and there were 37 pneumonia and influenza deaths.

TEAR OUT AND COPY FOR DISTRIBUTION TO PATIENTS

Vancomycin-Resistant Enterococci (VRE) Fact Sheet

What are enterococci?

Enterococci are bacteria that are normally found in the bowel and vagina of humans. When these bacteria get outside of these areas, they may cause urinary tract infections, wound infections or bloodstream infections. Enterococci are now the third most common cause of infections in hospitalized patients. These bacteria are often difficult to treat with antibiotics. However, one antibiotic that is normally effective is known as vancomycin.

How dangerous are enterococci?

They are fairly mild bacteria. Usually, they do not make healthy people sick. They can cause disease when people are very ill, like when the walls inside the bowel are damaged or when persons have devices such as catheters placed inside their bladders. Although infections with this bacteria usually clear up on their own without treatment, vancomycin-resistant enterococci cause special concern because the types of antibiotics available for treatment are limited. Many of these infections are often not treatable with the antibiotics that we have.

What are vancomycin-resistant enterococci (VRE)?

Vancomycin-resistant enterococci (VRE) are enterococci that can no longer be treated with vancomycin. This is primarily due to the high use of antibiotics. VRE now join the list of other bacteria that are difficult to treat with antibiotics.

Who gets ill with VRE?

Enterococci normally live in the bowel and genital tract. Therefore, most people have these bacteria inside of them without being ill. Those most likely to become ill with VRE are people who:

- Are older
- Have long hospital stays, especially in an intensive care unit
- Were hospitalized in the past
- Have taken antibiotics in the past
- Had prior surgery
- Have had medical devices such as urinary catheters

How is VRE passed from person to person?

These bacteria go from person to person on unwashed hands or objects. They are not carried in the air.

What can and should be done to limit the spread of VRE?

The most important control measure is good handwashing and personal cleaning habits. All care providers should routinely wash their hands before and after patient care and any time they are soiled.

Since these bacteria live in the bowel, they are found in human feces, but they may be carried in any human body fluid. Handwashing and wearing gloves should be a regular habit any time it is likely that hands will be soiled with these fluids. A gown or apron should be worn when it is likely that clothes will be soiled with another person's body fluids. Because these bacteria can be present in people without signs and symptoms of infection, it makes little sense to take "extra" precautions simply because the organism has been identified. In health care settings, the use of common sense precautions such as good handwashing and the proper use of barriers such as gloves and aprons has been found to work as well as more restrictive isolation systems.

What about cleaning and disinfection of the environment?

Since bacteria such as VRE may be passed on medical devices, methods for cleaning these devices should be in writing and should be followed. These bacteria have been found on surfaces in care areas. Although no special cleaning agents are necessary to remove them, good cleaning of surfaces in all patient care areas is important. Cleaning methods should emphasize "elbow grease".

Why do bacteria change so the antibiotics no longer work?

Some bacteria can naturally resist the effects of antibiotics. Other types of bacteria get used to living in the presence of antibiotics when antibiotics are taken often, taken when not needed or taken in the wrong doses. Later, when antibiotics are needed, the drug no longer kills these bacteria. Proper use can increase the length of time an antibiotic is useful. It is important that the public and the health care community do all they can to assure that antibiotics are ordered and used in a correct manner. Here are a few tips to increase the time that antibiotics remain effective:

- Do not pressure your doctor to prescribe antibiotics.
- Do not give your antibiotics to other people.
- Do not take antibiotics that have been sitting around the house unless prescribed by your doctor for a current illness.

Summary

1. An infection caused by bacteria that is difficult to treat with antibiotics (such as VRE) is no different than an infection caused by other bacteria, except that treatment options are limited.
2. The same infection control measures used to prevent the spread of all bacteria that can cause disease should be used to prevent the spread of bacteria like VRE.
3. The best way to prevent disease transmission is for clients and caregivers to follow good handwashing techniques and to use barriers such as gloves when soiling of the hands is likely. Other barriers such as gowns or aprons should be worn when soiling of clothing is likely.
4. Consistent and proper cleaning of surfaces like tabletops and medical devices is also important in removing these bacteria.

For more information about VRE or use of antibiotics, ask your physician or health care provider, infection control professional, pharmacist or contact:

Missouri Department of Health
Bureau of Communicable Disease Control
Ph: (573) 751-6113

Developed by Eddie Hedrick BS, MT(ASCP), CIC, Jo Micek RN, CIC and Chris Papasian PhD and approved by the Department of Health Advisory Committee on Infection Prevention and Control.

8/98

Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis

Reprinted from the Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports, Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis, May 15, 1998, Vol. 47, No. RR-7.

SUMMARY

This report updates and consolidates all previous PHS recommendations for the management of health-care workers (HCWs) who have occupational exposure to blood and other body fluids that may contain human immunodeficiency virus (HIV); it includes recommendations for HIV postexposure prophylaxis (PEP) and discusses the scientific rationale for PEP. The decision to recommend HIV postexposure prophylaxis must take into account the nature of the exposure (e.g., needlestick or potentially infectious fluid that comes in contact with a mucous membrane) and the amount of blood or body fluid involved in the exposure. Other considerations include pregnancy in the HCW and exposure to virus known or suspected to be resistant to antiretroviral drugs. Assessments of the risk for infection resulting from the exposure and of the infectivity of the exposure source are key determinants of offering PEP. Systems should be in place for the timely evaluation and management of exposed HCWs and for consultation with experts in the treatment of HIV when using PEP.

Recommendations for PEP have been modified to include a basic 4-week regimen of two drugs (zidovudine and lamivudine) for most HIV exposures and an expanded regimen that includes the addition of a protease inhibitor (indinavir or nelfinavir) for HIV exposures that pose an increased risk for transmission or where resistance to

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Occupational Exposures Also Pose Risk for Hepatitis B and Hepatitis C Infections

Health care workers (HCWs) who have an occupational exposure to a patient's blood or certain other body fluids can also be at risk for infection with other bloodborne pathogens such as hepatitis B virus (HBV) and hepatitis C virus (HCV). Recommendations for the management of HCWs who are exposed to these viruses have been published:

CDC. Immunization of health-care workers—recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC). MMWR 1997;46(no. RR-18):14-17, 22-23.
http://www.cdc.gov/epo/mmwr/preview/ind97_rr.html

CDC. Recommendations for follow-up of health-care workers after occupational exposure to hepatitis C virus. MMWR 1997;46(26):603–6.
http://www.cdc.gov/epo/mmwr/preview/index97.html

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one or more of the antiretroviral agents recommended for PEP is known or suspected. An algorithm is provided to guide clinicians and exposed health-care workers in deciding when to consider PEP.

Occupational exposures should be considered urgent medical concerns to ensure timely administration of PEP. Health-care organizations should have protocols that promote prompt reporting and facilitate access to postexposure care. Enrollment of HCWs in registries designed to assess side effects in HCWs who take PEP is encouraged.

INTRODUCTION

Although preventing blood exposures is the primary means of preventing occupationally acquired human immunodeficiency virus (HIV) infection, appropriate postexposure management is an important element of workplace safety. In January 1990, CDC issued a statement on the management of HIV exposures that included considerations for zidovudine (ZDV) use for postexposure prophylaxis (PEP) (1). At that time, data were insufficient to assess the efficacy of ZDV as a prophylactic agent in humans or the toxicity of this drug in persons not infected with HIV. Although there are still only limited data to assess safety and efficacy, additional information is now available that is relevant to this issue.

In December 1995, CDC published a brief report of a retrospective case-control study of health-care workers (HCWs) from France, the United Kingdom, and the United States exposed percutaneously to HIV; the study identified risk factors for HIV transmission and documented that the use of ZDV was associated with a decrease in the risk for HIV seroconversion (2). This information, along with data on ZDV efficacy in preventing perinatal transmission (3) and evidence that PEP prevented or ameliorated retroviral infection in some studies in animals (4), prompted a Public Health Service (PHS) interagency working group*, with expert consultation (5), in June 1996 to issue provisional recommendations for PEP for HCWs after occupational HIV exposure (6).

Since the provisional recommendations were released, several new antiretroviral drugs have been approved by the Food and Drug Administration (FDA), and more information is available about the use and safety of antiretroviral agents in exposed HCWs (7–10). In addition, questions have been raised about the use of chemoprophylaxis in situations not fully addressed in the 1996 recommendations, including when not to offer PEP, what to do when the source of exposure or the HIV status of the source person is unknown, how to approach PEP in HCWs who are or may be pregnant, and considerations for PEP regimens when the source person's virus is known or suspected to be resistant to one or more of the antiretroviral agents recommended for PEP.

In May 1997, a meeting of expert consultants, convened by CDC to consider the new information, prompted a PHS interagency working group** decision to issue updated recommendations. This document addresses the management of occupational exposure to HIV, including guidance in assessing and treating exposed HCWs, updates previous recommendations for occupational postexposure chemoprophylaxis, and updates and replaces all previous PHS guidelines and recommendations for occupational HIV exposure management for HCWs. Included in this document is an algorithm to guide decisions regarding the use of PEP for HIV exposures. The algorithm and these recommendations together address most issues that may be encountered during postexposure follow-up. As relevant information becomes available, updates of these recommendations will be published. Recommendations for non-occupational (e.g., sexual or pediatric) exposures are not addressed in these guidelines.

DEFINITIONS OF HEALTH-CARE WORKERS AND EXPOSURE

In this report, "health-care worker" (HCW) is defined as any person (e.g., an employee, student, contractor, attending clinician, public-safety worker, or volunteer) whose activities involve contact with patients or with blood or other body fluids from patients in a health-care or laboratory setting. An "exposure" that may place an HCW at risk for HIV infection and therefore requires consideration of PEP is defined as a percutaneous injury (e.g., a needlestick or cut with a sharp object), contact of mucous membrane or nonintact skin (e.g., when the exposed skin is chapped, abraded, or afflicted with dermatitis), or contact with intact skin when the duration of contact is prolonged (i.e., several minutes or more) or involves an extensive area, with blood, tissue, or other body fluids. Body fluids include a) semen, vaginal secretions, or other body fluids contaminated with visible blood that have been implicated in the transmission of HIV infection (11,12); and b) cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids, which have an undetermined risk for transmitting HIV (11). In addition, any direct contact (i.e., without barrier protection) to concentrated HIV in a research laboratory or production facility is considered an "exposure" that requires clinical evaluation and consideration of the need for PEP.

Although one non-occupational episode of HIV transmission has been attributed to contact with blood-contaminated saliva (13), this incident involved intimate kissing between sexual partners

* This interagency working group comprised representatives of CDC, the Food and Drug Administration, the Health Resources and Services Administration, and the National Institutes of Health.

** This interagency working group comprised representatives of CDC, FDA, and the National Institutes of Health. Information included in these recommendations may not represent FDA approval or approved labeling for the particular product or indications in question. Specifically the terms "safe" and "effective" may not be synonymous with the FDA-defined legal standards for product approval.

and is not similar to contact with saliva that may occur during the provision of health-care services. Therefore, in the absence of visible blood in the saliva, exposure to saliva from a person infected with HIV is not considered a risk for HIV transmission; also, exposure to tears, sweat, or non-bloody urine or feces does not require postexposure follow-up. [†]

Human breast milk has been implicated in perinatal transmission of HIV. However, occupational exposure to human breast milk has not been implicated in HIV transmission to HCWs. Moreover, the contact HCWs may have with human breast milk is quite different from perinatal exposure and does not require postexposure follow-up.

BACKGROUND

The rationale is provided here for the postexposure management and prophylaxis recommendations given at the end of the document. Additional details concerning the risk for occupational HIV transmission to HCWs and management of occupational HIV exposures are available elsewhere (16–18).

Risk for Occupational Transmission of HIV to HCWs

Prospective studies of HCWs have estimated that the average risk for HIV transmission after a percutaneous exposure to HIV-infected blood is approximately 0.3% (95% confidence interval [CI]=0.2%–0.5%) (16) and after a mucous membrane exposure is 0.09% (95% CI=0.006%–0.5%) (19). Although episodes of HIV transmission after skin exposure have been documented (20), the average risk for transmission by this route has not been precisely quantified because no HCWs enrolled in prospective studies have seroconverted after an isolated skin exposure. The risk for transmission is estimated to be less than the risk for mucous membrane exposures (21). The risk for transmission after exposure to fluids or tissues other than HIV-infected blood also has not been quantified.

As of June 1997, CDC has received reports of 52 U.S. HCWs with documented HIV seroconversion temporally associated with an occupational HIV exposure. An additional 114 episodes in HCWs are considered possible occupational HIV transmissions; these workers reported that their infection was occupationally acquired and no other risk for HIV infection was identified, but transmission of infection after a specific exposure was not documented (22). Of the 52 documented episodes, 47 HCWs were exposed to HIV-infected blood, one to a visibly bloody body fluid, one to an unspecified fluid, and three to concentrated virus in a laboratory. Forty-five exposures were percutaneous, and five were mucocutaneous; one HCW had both a percutaneous and a mucocutaneous exposure. The route of exposure for one person exposed to concentrated virus is uncertain. Of the percutaneous exposures, the objects involved included a hollow-bore needle (41), a broken glass vial (two), a scalpel (one), and an unknown sharp object (one) (CDC, unpublished data, 1998).

Epidemiologic and laboratory studies suggest that several factors may affect the risk for HIV transmission after an occupational exposure. The one retrospective case-control study of HCWs who had percutaneous exposure to HIV found that the risk for HIV transmission was increased with exposure to a larger quantity of blood from the source patient as indicated by a) a device visibly contaminated with the patient's blood, b) a procedure that involved a needle placed directly in a vein or artery, or c) a deep injury (23). (A laboratory study that demonstrated that more blood is transferred by deeper injuries and hollow-bore needles lends further support for the observed variation in risk related to blood quantity [24]). The risk also was increased for exposure to blood from source patients with terminal illness, possibly reflecting either the higher titer of HIV in blood late in the course of AIDS or other factors (e.g., the presence of syncytia-inducing strains of HIV). It was estimated that the risk for HIV transmission from exposures that involve a larger volume of blood, particularly when the source patient's viral load is probably high, exceeds the average risk of 0.3% (23).

The utility of viral load measurements from a source patient as a surrogate for estimating the viral titer for assessing transmission risk is not known. Plasma viral load measurement (e.g., HIV RNA) reflects only the level of cell-free virus in the peripheral blood. This measurement does not reflect the level of cell-associated virus in the peripheral blood or the level of virus in other body compartments (e.g., lymphatic tissue). Although a lower viral load, or results that are below the limits of viral quantification, in the peripheral blood probably indicates a lower titer exposure, it does not rule out the possibility of transmission; HIV transmission from persons with a plasma viral load below the limits of viral quantification (based on the assay used at the time) has been reported in instances of mother-to-infant transmission (25, 26) and in one HCW seroconversion (J.L. Gerberding, San Francisco General Hospital, unpublished data, May 1997).

There is some evidence that host defenses also may influence the risk for HIV infection. In one small study, HIV-exposed but uninfected HCWs demonstrated an HIV-specific cytotoxic T-lymphocyte (CTL) response when

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[†] Although exposure to these body substances generally is not considered a risk for occupational HIV transmission, this does not negate the importance of handwashing and appropriate glove use when contacting these body substances. Handwashing and appropriate glove use are part of standard precautions for infection control to prevent transmission of nosocomial and community-acquired pathogens and are required for compliance with the Occupational Safety and Health Administration bloodborne pathogen standard (14,15). In addition, postexposure evaluation for hepatitis B (and possibly hepatitis C) should be provided if contact with saliva includes a possible portal of entry (i.e., nonintact skin, mucous membrane, or percutaneous injury).

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peripheral blood mononuclear cells were stimulated in vitro with HIV mitogens (27). Similar CTL responses have been observed in other populations with repeated HIV exposure without resulting infection (28–33). Among several possible explanations for this observation, one is that the host immune response sometimes may be able to prevent establishment of HIV infection after a percutaneous exposure; another is that the CTL response simply may be a marker for exposure.

HIV Seroconversion in HCWs

Data on the timing and clinical characteristics of seroconversion in HIV-exposed HCWs are limited by the infrequency of infection following occupational exposure, variations in postexposure testing intervals, and differences over time in the sensitivity of HIV-antibody testing methods. Among the HCWs with documented seroconversions reported to CDC for whom data are available, 81% experienced a syndrome compatible with primary HIV infection a median of 25 days after exposure (CDC, unpublished data, 1998). In a recent analysis of 51 seroconversions in HCWs, the estimated median interval from exposure to seroconversion was 46 days (mean: 65 days); an estimated 95% seroconverted within 6 months after the exposure (34). These data suggest that the time course of HIV seroconversion in HCWs is similar to that in other persons who have acquired HIV through non-occupational modes of transmission (35).

Three instances of delayed HIV seroconversion occurring in HCWs have been reported; in these instances, the HCWs tested negative for HIV antibodies >6 months postexposure but were seropositive within 12 months after the exposure (36,37; J.L. Gerberding, San Francisco General Hospital, unpublished data, May 1997). DNA sequencing confirmed the source of infection in one instance. Two of the delayed seroconversions were associated with simultaneous exposure to hepatitis C virus (HCV) (37; J.L. Gerberding, San Francisco General Hospital, unpublished data, May 1997). In one case, coinfection was associated with a rapidly fatal HCV disease course (37); however, it is not known whether HCV directly influences the risk for or course of HIV infection or is a marker for other exposure-related factors.

Rationale for PEP

Considerations that influence the rationale and recommendations for PEP include the pathogenesis of HIV infection, particularly the time course of early infection; the biologic plausibility that infection can be prevented or ameliorated by using antiretroviral drugs and direct or indirect evidence of the efficacy of specific agents used for prophylaxis; and the risk/benefit of PEP to exposed HCWs. The following discussion considers each of these issues.

Role of Pathogenesis in Considering Antiretroviral Prophylaxis

Information about primary HIV infection indicates that systemic infection does not occur immediately, leaving a brief "window of opportunity" during which postexposure antiretroviral intervention may modify viral replication. Data from studies in animal models and in vitro tissue studies suggest that dendritic cells in the mucosa and skin are the initial targets of HIV infection or capture and have an important role in initiating HIV infection of CD4+ T-cells in regional lymph nodes (38). In a primate model of simian immunodeficiency virus (SIV) infection, infection of dendritic-like cells occurred at the site of inoculation during the first 24 hours following mucosal exposure to cell-free virus. During the subsequent 24–48 hours, migration of these cells to regional lymph nodes occurred, and virus was detectable in the peripheral blood within 5 days (39). HIV replication is rapid (generation time: 2.5 days) and results in bursts of up to 5,000 viral particles from each replicating cell (40; M.S. Saag, University of Alabama, personal communication, September 1997). The exponential increase in viral burden continues unless controlled by the immune system or other mechanisms (e.g., exhaustion of available target CD4+ T-cells). Theoretically, initiation of antiretroviral PEP soon after exposure may prevent or inhibit systemic infection by limiting the proliferation of virus in the initial target cells or lymph nodes.

Efficacy of Antiretrovirals for PEP

Studies in animals and humans provide direct and indirect evidence of the efficacy of antiretroviral drugs as agents for postexposure prophylaxis. In human studies and in most animal studies, ZDV was the antiretroviral agent used for prophylaxis (26,41–54). However, in more recent animal studies, newer agents also have been reported to be effective (55,56).

Data from animal studies have been difficult to interpret, in part because of problems identifying a comparable animal model for humans. Most studies use a higher inoculum for exposure than would be expected in needlestick injuries. Among the animal studies, differences in controlled variables (e.g., choice of viral strain [based on the animal model used], inoculum size, route of inoculation, time of prophylaxis initiation, and drug regimen) make attempts to apply these results to humans difficult. In the animal studies that showed efficacy of pre-exposure and/or postexposure prophylaxis, reported outcomes (4,57) have included a) suppression of viremia or delayed antigenemia (41–47); b) drug-facilitated vaccine-type response (i.e., chemoprophylaxis sufficiently inhibited viral replication to permit formation of a long-lasting, protective cellular immune response) (48–56); and c) definitive prevention of infection (i.e., chemoprophylactic efficacy) (41,52–54). More recent refinements in methodology have enabled studies more relevant to humans; in particular, the viral inocula used in animal studies have been reduced

to levels more analogous to human exposures (54,56). The results of these studies provide additional evidence of postexposure chemoprophylactic efficacy.

In studies of HIV-2 or SIV in nonhuman primates in which ZDV or 3'-fluorothymidine was used, suppression or delay of antigenemia was the most common outcome; prevention of infection was infrequent (43,52,58–60). However, two other antiretroviral agents, 2',3'-dideoxy-3'-hydroxymethyl cytidine (BEA-005) and (R)-9-(2-phosphonylmethoxypropyl) adenine (PMPA), used to study PEP in primates have been more effective in preventing infection. When PMPA was administered 48 hours before, 4 hours after, or 24 hours after intravenous SIV inoculation to long-tailed macaques, a 4-week regimen prevented infection in all treated animals (55). A 3-day regimen of BEA-005 prevented SIV infection in 12 of 12 pigtailed macaques when administered 1–8 hours after intravenous inoculation; infection also was prevented in four of four animals that received 3 days of BEA-005 within 10 minutes after HIV-2 inoculation (56).

Animal studies have demonstrated that early initiation of PEP and small inoculum size are correlates of successful PEP. ZDV initiated 1 hour or 24 hours after intravenous exposure to a rapidly lethal variant of SIV in pigtailed macaques prevented infection in one of three animals and modified SIV disease in three of six animals, respectively; PEP initiated at 72 hours had no effect (54). In macaques administered ZDV or BEA-005 1 to 72 hours after SIV intravenous challenge, earlier initiation of PEP was correlated with delayed onset and peak of antigenemia, decreased duration of antigenemia, and reduction in SIV serum titer; the most potent effect was evident when PEP was initiated within 8 hours of exposure (43,56). Studies in primates and murine and feline animal models have demonstrated that larger inocula decrease prophylactic efficacy (47,48,53,60). In addition, delaying initiation, shortening the duration, or decreasing the antiretroviral dose of PEP, individually or in combination, decreased prophylactic efficacy (42,43,45,47,50,55).

There is little information with which to assess the efficacy of PEP in humans. Seroconversion is infrequent after an occupational exposure to HIV-infected blood; therefore a prospective trial would need to enroll many thousands of exposed HCWs to achieve the statistical power necessary to directly demonstrate PEP efficacy. During 1987–1989, the Burroughs-Wellcome Company sponsored a prospective placebo-controlled clinical trial among HCWs to evaluate 6 weeks of ZDV prophylaxis; however, this trial was terminated prematurely because of low enrollment (61). Because of current indirect evidence of PEP efficacy, it is unlikely that a placebo-controlled trial in HCWs would ever be feasible.

In the retrospective case-control study of HCWs, after controlling for other risk factors for HIV transmission, the risk for HIV infection among HCWs who used ZDV as PEP was reduced by approximately 81% (95% CI=43%–94%) (23). In addition, in a randomized, controlled, prospective trial (AIDS Clinical Trial Group [ACTG] protocol 076) in which ZDV was administered to HIV-infected pregnant women and their infants, the administration of ZDV during pregnancy, labor, and delivery and to the infant reduced transmission by 67% (3). Only 9%–17% (depending on the assay used) of the protective effect of ZDV was explained by reduction of the HIV titer in the maternal blood, suggesting that ZDV prophylaxis in part involves a mechanism other than the reduction of maternal viral burden (26).

The limitations of all of these studies must be considered when reviewing evidence of PEP efficacy. The extent to which data from animal studies can be extrapolated to humans is largely unknown, and the exposure route for mother-to-infant HIV transmission is not similar to occupational exposures; therefore these findings may not reflect a similar mechanism of ZDV prophylaxis in HCWs. Although the results of the retrospective case-control study of HCWs suggest PEP efficacy, the limitations of that study include the small number of cases studied and the use of cases and controls from different cohorts.

Failure of ZDV PEP to prevent HIV infection in HCWs has been reported in at least 14 instances (62–64; G. Ippolito, AIDS Reference Center, Rome, Italy, and J. Heptonstall, Communicable Disease Surveillance Center, London, United Kingdom, personal communication, 1997). Although eight of the 13 source patients had taken ZDV, laboratory assessment for ZDV resistance of the virus from the source patient was performed in only three instances, two of which demonstrated reduced susceptibility to ZDV. In addition to possible exposure to a ZDV-resistant strain of HIV, other factors that may have contributed to the apparent failures in these instances may include a high titer and/or large inoculum exposure, delayed initiation and/or short duration of PEP, and possible factors related to the host (e.g., cellular immune system responsiveness) and/or to the source patient's virus (e.g., presence of syncytia-forming strains) (62).

Antiretroviral Agents for PEP

Several antiretroviral agents from at least three classes of drugs are available for the treatment of HIV disease. These include the nucleoside analogue reverse transcriptase inhibitors (NRTIs), nonnuceloside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) (See Appendix). Among these drugs, ZDV (an NRTI) is the only agent shown to prevent HIV transmission in humans (2,3). Although there are theoretical concerns that the increased prevalence of resistance to ZDV may diminish its utility for PEP (65), no data are available to assess whether this is a factor for consideration. Clinical data from the ACTG protocol

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076 study documented that despite genotypic evidence of maternal ZDV resistance, ZDV prevented perinatal transmission (66). Thus, based on the available information, it is still reasonable that ZDV should continue to be the first drug of choice for PEP regimens.

There are no data to directly support the addition of other antiretroviral drugs to ZDV to enhance the effectiveness of the PEP regimen. However, in HIV-infected patients, combination regimens have proved superior to monotherapy regimens in reducing HIV viral load (67, 68). Thus, theoretically a combination of drugs with activity at different stages in the viral replication cycle (e.g., NRTIs with a PI) could offer an additive preventive effect in PEP, particularly for occupational exposures that pose an increased risk for transmission.

Determining which agents and how many agents to use or when to alter a PEP regimen is largely empiric. Guidelines for the treatment of early HIV infection recommend the use of three drugs (two NRTIs and a PI) (69); however, the applicability of these recommendations to PEP remains unknown. In addition, the routine use of three drugs for all occupational HIV exposures may not be needed. Although the use of a highly potent regimen can be justified for exposures that pose an increased risk for transmission, it is uncertain whether the potential additional toxicity of a third drug is justified for lower-risk exposures. For this reason, the recommendations at the end of this report provide guidance for two- and three-drug PEP regimens that are based on the level of risk for HIV transmission represented by the exposure.

NRTIs that can be considered for use with ZDV for PEP are lamivudine (3TC), didanosine (ddI), and zalcitabine, each of which has been included in recommended regimens that include ZDV (69). In previous CDC recommendations, 3TC was recommended as a second agent for PEP based on greater antiretroviral activity of the ZDV/3TC combination and its activity against many ZDV-resistant HIV strains without substantially increased toxicity (6). Also, data suggest that ZDV-resistant mutations develop more slowly in patients receiving the ZDV/3TC combination than those receiving ZDV alone (70), and in vitro studies indicate that the mutation associated with 3TC resistance may be associated with reversal of ZDV phenotypic resistance (71). No additional information has emerged to warrant altering the original recommendation of 3TC as the second agent for PEP. In addition, because ZDV and 3TC are available in a combination formulation (Combivir™, manufactured by Glaxo Wellcome, Inc., Research Triangle Park, NC), the use of 3TC may be more convenient for HCWs. However, individual clinicians may prefer other NRTIs or combinations of other antiretroviral agents based on local knowledge and experience in treating HIV infection and disease.

The addition of a PI as a third drug for PEP following high-risk exposures is based on the site of activity in the replication cycle (i.e., after viral integration has occurred) and demonstrated effectiveness in reducing viral burden. Previously, indinavir (IDV) was recommended as the PI for PEP because of its increased bioavailability when compared with saquinavir and its more favorable immediate toxicity profile compared with ritonavir (72). In addition, requirements for dose escalation when initiating ritonavir make it less practical for use in PEP. Since the 1996 PEP recommendations were published, nelfinavir (NEL) was approved for use by FDA and is now included in regimens recommended for the treatment of primary HIV infection (69). Also, FDA recently approved a soft-gel formulation of saquinavir (Fortovase™, manufactured by Hoffmann-LaRoche, Inc., Nutley, New Jersey) that has improved bioavailability relative to its hard-gel formulation (Invirase™, manufactured by Hoffmann-LaRoche, Inc.). However, the recommended dose of soft-gel saquinavir (1200 mg three times a day) is twice that of the hard-gel formulation (600 mg three times a day) and necessitates taking 18 pills a day, a factor that may influence HCW compliance if used for PEP. Based on these considerations, either IDV or NEL is recommended as first choice for inclusion in an expanded PEP regimen. If saquinavir is preferred by the prescribing physician, the soft-gel formulation (Fortovase™) should be used. Also, differences in the side effects associated with IDV and NEL, discussed below, may influence which of these agents is selected in a specific situation.

The NNRTIs (i.e., nevirapine and delavirdine) have not been included in these recommended regimens for PEP. As a class of antiretroviral agents, the NNRTIs are fast-acting and very potent, making them appealing in concept for PEP. In addition, there is some evidence of prophylactic efficacy (73). However, concerns about side effects and the availability of alternative agents argue against routinely using this class of drugs for initial PEP, although with expert consultation, an NNRTI might be considered.

Side Effects and Toxicity of Antiretroviral Agents

An important goal of PEP is to encourage and facilitate compliance with a 4-week PEP regimen. Therefore, the toxicity profile of antiretroviral agents, including the frequency, severity, duration, and reversibility of side effects, is a relevant consideration. All of the antiretroviral agents have been associated with side effects (See Appendix). However, studies of adverse events have been reported primarily for persons with advanced disease (and longer treatment courses) and therefore may not reflect the experience of persons with less advanced disease or those who are uninfected (74). Side effects associated with many of the NRTIs (e.g., ZDV or ddI) are chiefly gastrointestinal (e.g., nausea or diarrhea), and in general the incidence of adverse effects has not been greater when these agents are used in combination (72).

All of the approved PIs may have potentially serious drug interactions when used with certain other drugs, requiring careful evaluation of concomitant medications being used by a HCW before prescribing a PI and close monitoring for toxicity when a HCW is receiving one of these drugs (See Appendix). PIs may inhibit the metabolism of nonsedating antihistamines and other hepatically metabolized drugs; NEL and ritonavir may accelerate the clearance of certain drugs, including oral contraceptives (requiring alternative or additional contraceptive measures for women taking these drugs). The use of PIs also has been associated with new onset of diabetes mellitus, hyperglycemia, diabetic ketoacidosis, and exacerbation of preexisting diabetes mellitus (75–77). Nephrolithiasis has been associated with IDV use (including in HCWs using the drug for PEP) (8); however, the incidence of this potential complication may be limited by drinking at least 48 oz (1.5 L) of fluid per 24-hour period (e.g., six 8 oz glasses of water throughout the day) (72). Rare cases of hemolytic anemia also have been associated with the use of IDV. NEL, saquinavir, and ritonavir have been associated with the development of diarrhea; however, this side effect usually responds to treatment with antimotility agents that can be prescribed for use, if necessary, at the time any one of these drugs is prescribed for PEP. The manufacturer's package insert should always be consulted for questions about potential drug interactions.

Among HCWs receiving ZDV PEP, usually at doses of 1,000–1,200 mg per day (i.e., higher than the currently recommended dose), 50%–75% reported one or more subjective complaints and approximately 30% discontinued the drug because of symptoms (7,78,79). Common symptoms included nausea, vomiting, malaise or fatigue, headache, or insomnia. Mild decreases in hemoglobin and absolute neutrophil count also were observed. All side effects were reversed when PEP was discontinued.

Preliminary information about HCWs receiving combination drugs for PEP (usually ZDV plus 3TC with or without a PI) suggests that approximately 50%–90% of HCWs report subjective side effects that caused 24%–36% to discontinue PEP (8–10). One study documented that combination regimens that included ZDV at a lower dose (600 mg per day) were better tolerated than high-dose ZDV used alone (1,000–1,200 mg per day) (10). However, serious side effects, including nephrolithiasis, hepatitis, and pancytopenia, have been reported with the use of combination drugs for PEP (9,80; J.L. Gerberding, San Francisco General Hospital, personal communication, May 1997).

Resistance to Antiretroviral Agents

Known or suspected resistance of the source virus to antiretroviral agents, particularly to one or more agents that might be included in a PEP regimen, is a concern for those making decisions about PEP. Resistance of HIV has been reported with all available antiretroviral agents (65). However, the relevance of exposure to a resistant virus is not understood. Although transmission of resistant strains has been reported (81–85), in the perinatal clinical trial that studied vertical HIV transmission (ACTG protocol 076), ZDV prevented perinatal transmission despite genotypic resistance of HIV to ZDV in the mother (66). In addition, patients generally take more than one antiretroviral drug and, unless testing is performed, often it is difficult to know to which drug(s) resistance exists. The complexity of this issue is further compounded by the frequency of cross-resistance within drug classes.

Resistance should be suspected in source patients when there is clinical progression of disease or a persistently increasing viral load and/or a decline in CD4 T-cell count despite therapy, or a lack of virologic response to a change in therapy. Nevertheless, in this situation it is unknown whether a modification in the PEP regimen is necessary or will influence the outcome of an occupational exposure.

Antiretroviral Drugs in Pregnancy

Considerations for the use of antiretroviral drugs in pregnancy include their potential effect on the pregnant woman and on her fetus or neonate. The pharmacokinetics of antiretroviral drugs has not been completely studied in pregnant women. Some of the antiretroviral drugs are known to cross the placenta, but data for humans are not yet available for others (particularly the PIs). In addition, data are limited on the potential effects of antiretroviral drugs on the developing fetus or neonate (86). Decisions on the use of specific drugs in pregnancy also are influenced by whether a drug has specific adverse effects or might further exacerbate conditions associated with pregnancy, (e.g., drugs that cause nausea may be less tolerated when superimposed on the nausea normally associated with pregnancy).

There are data on both ZDV and 3TC from clinical trials in HIV-infected pregnant women. The most extensive experience has been with the use of ZDV after 14 weeks of gestation in pregnant HIV-infected women in phase I studies and the perinatal ACTG protocol 076 (4,87). The dose of ZDV for pregnant women is the same as that in nonpregnant persons, and ZDV appears safe and well tolerated in both women and their infants who have had a follow-up period of several years (88–90). Data from the Antiretroviral Pregnancy Registry have not documented an increased risk for birth defects in infants with in utero exposure to ZDV (91). There are limited data on use of 3TC alone or in combination with ZDV in late gestation in pregnant HIV-infected women. As with ZDV, the pharmacokinetics and dose of 3TC appear to be similar to those for nonpregnant persons. The drug appears safe during pregnancy for women and infants, although long-term safety is not known (92,93).

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Carcinogenicity and/or mutagenicity is evident in several in vitro screening tests for ZDV and all other FDA-licensed nucleoside antiretroviral drugs. In some in vivo rodent studies, high-dose lifetime continuous ZDV exposure (94) or very high dose in utero ZDV exposure has been associated with the development of tumors in adult females or their offspring (95,96). The relevance of these animal data to humans is unknown. However, in 1997 an independent panel reviewed these data and concluded that the known benefits of ZDV in preventing perinatal transmission, where the risk for transmission without ZDV is 25%–30%, outweigh the hypothetical concerns about transplacental carcinogenesis (97).

No data are available regarding pharmacokinetics, safety, or tolerability of any of the PIs in pregnant women. The use of PIs in HIV-infected persons has been associated with hyperglycemia; it is unknown whether the use of these agents during pregnancy will exacerbate the risk for pregnancy-associated hyperglycemia. Therefore, close monitoring of glucose levels and careful instruction regarding symptoms related to hyperglycemia are recommended for pregnant HCWs receiving a PI for PEP. IDV is associated with infrequent side effects in adults (i.e., hyperbilirubinemia and renal stones) that could be problematic for the newborn. As the half-life of IDV in adults is short, these concerns may be relevant only if the drug is administered shortly before delivery.

RECOMMENDATIONS FOR THE MANAGEMENT OF POTENTIALLY EXPOSED HCWs

Health-care organizations should make available to their workers a system that includes written protocols for prompt reporting, evaluation, counseling, treatment, and follow-up of occupational exposures that may place HCWs at risk for acquiring any bloodborne infection, including HIV. Employers also are required to establish exposure-control plans, including postexposure follow-up for their employees, and to comply with incident reporting requirements mandated by the Occupational Safety and Health Administration (15). Access to clinicians who can provide postexposure care should be available during all working hours, including nights and weekends. Antiretroviral agents for PEP should be available for timely administration (i.e., either by providing access to PEP drugs on site or creating links with other facilities or providers to make them available offsite). Persons responsible for providing postexposure counseling should be familiar with evaluation and treatment protocols and the facility's procedures for obtaining drugs for PEP.

HCWs should be educated to report occupational exposures immediately after they occur, particularly because PEP is most likely to be effective if implemented as soon after the exposure as possible (41,55,56). HCWs who are at risk for occupational exposure to HIV should be taught the principles of postexposure management, including options for PEP, as part of job orientation and ongoing job training.

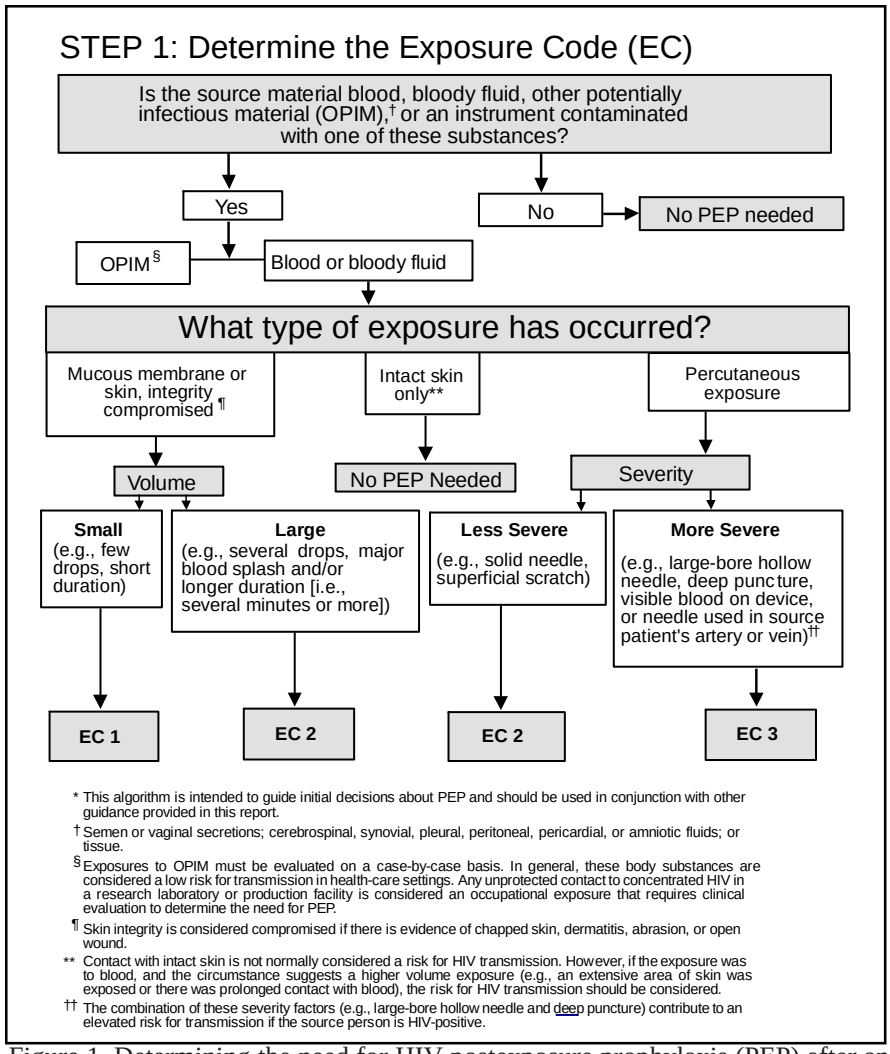

Figure 1. Determining the need for HIV postexposure prophylaxis (PEP) after an occupational exposure Step 1:*

Exposure Report

If an occupational exposure occurs, the circumstances and postexposure management should be recorded in the HCW's confidential medical record (usually on a form the facility designates for this purpose). Relevant information includes

- date and time of exposure;
- details of the procedure being performed, including where and how

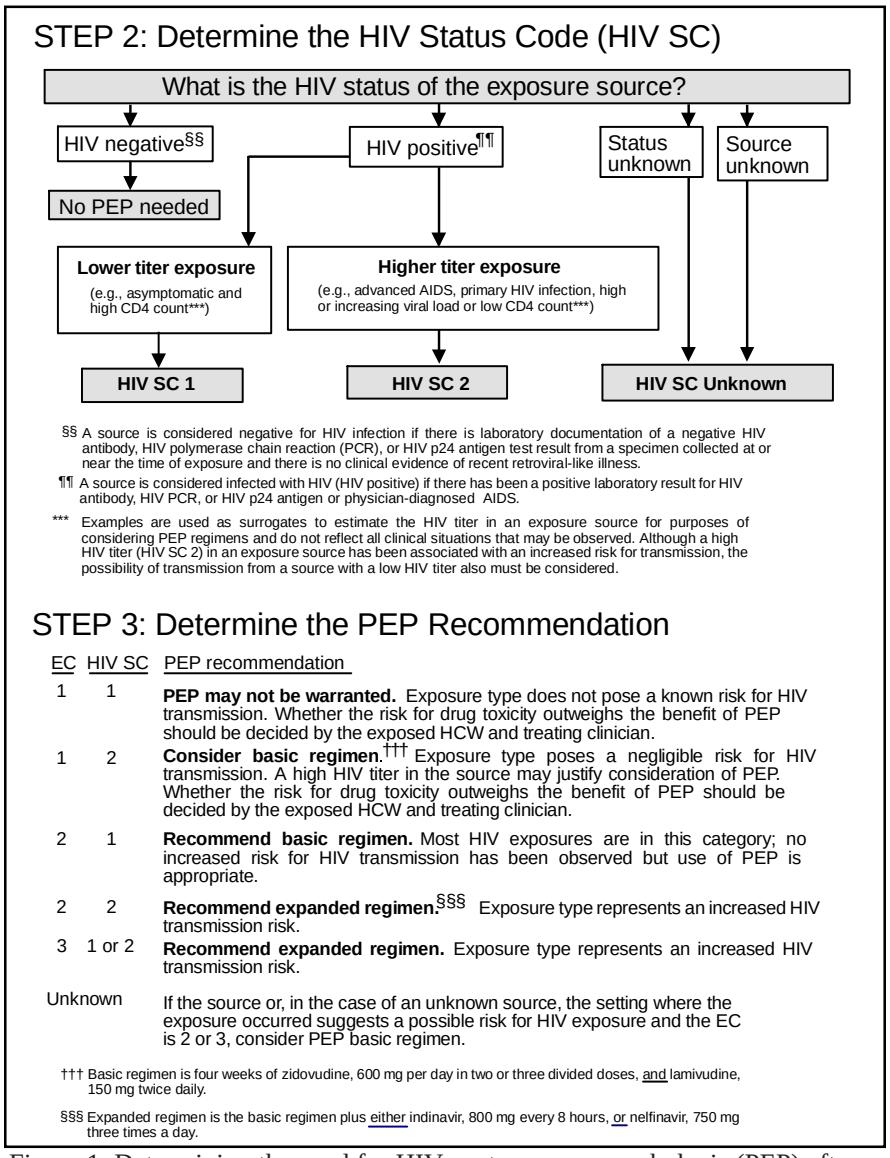

Figure 1. Determining the need for HIV postexposure prophylaxis (PEP) after an occupational exposure Steps 2 and 3:*

the exposure occurred, and if the exposure was related to a sharp device, the type of device and how and when in the course of handling the device the exposure occurred;

- details of the exposure, including the type and amount of fluid or material and the severity of the exposure (e.g., for a percutaneous exposure, depth of injury and whether fluid was injected; or for a skin or mucous-membrane exposure, the estimated volume of material and duration of contact and the condition of the skin [e.g., chapped, abraded, or intact]);
- details about the exposure source (i.e., whether the source material contained HIV or other bloodborne pathogen[s]), and if the source is an HIV-infected person, the stage of disease, history of antiretroviral therapy, and viral load, if known; and
- details about counseling, postexposure management, and follow-up.

Exposure Management

Treatment of an Exposure Site

Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water; mucous membranes should be flushed with water. There is no evidence that the use of antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk for HIV transmission. However, the use of antiseptics is not contraindicated. The application of caustic agents (e.g., bleach) or the injection of antiseptics or disinfectants into the wound is not recommended.

Assessment of Infection Risk

After an occupational exposure, the source-person and the exposed HCW should be evaluated to determine the need for HIV PEP. Follow-up for hepatitis B virus and hepatitis C virus infections also should be conducted in accordance with previously published CDC recommendations (98,99).

Evaluation of exposure. The exposure should be evaluated for potential to transmit HIV based on the type of body substance involved and the route and severity of the exposure. Exposures to blood, fluid containing visible blood, or other potentially infectious fluid (including semen; vaginal secretions; and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids) or tissue through a percutaneous injury (i.e., needlestick or other penetrating sharps-related event) or through contact with a mucous membrane are situations that pose a risk for bloodborne transmission and require further evaluation (Figure 1). In addition, any direct contact (i.e., personal protective equipment either was not used or was ineffective in protecting skin or mucous membranes) with concentrated HIV in a research laboratory or production facility is considered an exposure that requires clinical evaluation to assess the need for PEP.

For skin exposures, follow-up is indicated if it involves direct contact with a body fluid listed above and there is evidence of compromised skin integrity (e.g., dermatitis, abrasion, or open wound). However, if the contact is prolonged or involves a large area of intact skin, postexposure follow-up may

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be considered on a case-by-case basis or if requested by the HCW.

For human bites, the clinical evaluation must consider possible exposure of both the bite recipient and the person who inflicted the bite. HIV transmission only rarely has been reported by this route (100,101; CDC, unpublished data, 1998). If a bite results in blood exposure to either person involved, postexposure follow-up, including consideration of PEP, should be provided.

Evaluation and testing of an exposure source. The person whose blood or body fluids are the source of an occupational exposure should be evaluated for HIV infection. Information available in the medical record at the time of exposure (e.g., laboratory test results, admitting diagnosis, or past medical history) or from the source person may suggest or rule out possible HIV infection. Examples of information to consider when evaluating an exposure source for possible HIV infection include laboratory information (e.g., prior HIV testing results or results of immunologic testing [e.g., CD4+ count]), clinical symptoms (e.g., acute syndrome suggestive of primary HIV infection or undiagnosed immunodeficiency disease), and history of possible HIV exposures (e.g., injecting-drug use, sexual contact with a known HIV-positive partner, unprotected sexual contact with multiple partners [heterosexual and/or homosexual], or receipt of blood or blood products before 1985).

If the source is known to have HIV infection, available information about this person's stage of infection (i.e., asymptomatic or AIDS), CD4+ T-cell count, results of viral load testing, and current and previous antiretroviral therapy, should be gathered for consideration in choosing an appropriate PEP regimen. If this information is not immediately available, initiation of PEP, if indicated, should not be delayed; changes in the PEP regimen can be made after PEP has been started, as appropriate.

If the HIV serostatus of the source person is unknown, the source person should be informed of the incident and, if consent is obtained, tested for serologic evidence of HIV infection. If consent cannot be obtained (e.g., patient is unconscious), procedures should be followed for testing source persons according to applicable state and local laws. Confidentiality of the source person should be maintained at all times.

HIV-antibody testing of an exposure source should be performed as soon as possible. Hospitals, clinics, and other sites that manage exposed HCWs should consult their laboratories regarding the most appropriate test to use to expedite these results. An FDA-approved rapid HIV-antibody test kit should be considered for use in this situation, particularly if testing by enzyme immunoassay (EIA) cannot be completed within 24–48 hours. Repeatedly reactive results by EIA or rapid HIV-antibody tests are considered highly suggestive of infection, whereas a negative result is an excellent indicator of the absence of HIV antibody. Confirmation of a reactive result by Western blot or immunofluorescent antibody is not necessary for making initial decisions about postexposure management but should be done to complete the testing process.

If the source is HIV seronegative and has no clinical evidence of acquired immunodeficiency syndrome (AIDS) or symptoms of HIV infection, no further testing of the source is indicated. It is unclear whether follow-up testing of a source who is HIV negative at the time of exposure, but recently (i.e., within the last 3–6 months) engaged in behaviors that pose a risk for HIV transmission, is useful in postexposure management of HCWs; HCWs who become infected generally seroconvert before repeat testing of a source would normally be performed.

If the exposure source is unknown, information about where and under what circumstances the exposure occurred should be assessed epidemiologically for risk for transmission of HIV. Certain situations, as well as the type of exposure, may suggest an increased or decreased risk; an important consideration is the prevalence of HIV in the population group (i.e., institution or community) from which the contaminated source material is derived. For example, an exposure that occurs in a geographic area where injecting-drug use is prevalent or on an AIDS unit in a health-care facility would be considered epidemiologically to have a higher risk for transmission than one that occurs in a nursing home for the elderly where no known HIV-infected residents are present. In addition, exposure to a blood-filled hollow needle or visibly bloody device suggests a higher-risk exposure than exposure to a needle that was most likely used for giving an injection. Decisions regarding appropriate management should be individualized based on the risk assessment.

HIV testing of needles or other sharp instruments associated with an exposure, regardless of whether the source is known or unknown, is not recommended. The reliability and interpretation of findings in such circumstances are unknown.

Clinical Evaluation and Baseline Testing of Exposed HCWs

Exposed HCWs should be evaluated for susceptibility to bloodborne pathogen infections. Baseline testing (i.e., testing to establish serostatus at the time of exposure) for HIV antibody should be performed. If the source person is seronegative for HIV, baseline testing or further follow-up of the HCW normally is not necessary. If the source person has recently engaged in behaviors that are associated with a risk for HIV transmission, baseline and follow-up HIV-antibody testing (e.g., 3 and/or 6 months postexposure) of the HCW should be considered. Serologic testing should be made available to all HCWs who are concerned that they may have been exposed to HIV.

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1998 Guidelines for Treatment of Sexually Transmitted Diseases

(Continued from the January-February and March-April 1998 issues of the *Missouri Epidemiologist*)

Physicians and other health-care providers have a critical role in preventing and treating sexually transmitted diseases (STDs). The following recommendations for the treatment of STDs, which were developed by the Centers for Disease Control and Prevention (CDC) in consultation with a group of outside experts, are intended to assist with that effort.

The recommendations, which update those released by CDC in 1993, were reprinted from CDC's *Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports*, Vol. 47, No. RR-1, January 23, 1998. This issue of the *Missouri Epidemiologist* contains those sections of the guidelines which relate to human immunodeficiency virus (HIV) infection and human papillomavirus (HPV) infection. Those sections relating to diseases characterized by urethritis and cervicitis were reprinted in the January-February 1998 issue and diseases characterized by genital ulcers and congenital syphilis in the March-April 1998 issue.

A full copy of the guidelines and reference list in pdf format can be found on CDC's Division of STD Prevention Home Page at **http://www.cdc.gov/nchstp/dstd/dstdp.htm.**

If you have questions regarding these guidelines, please contact DOH's Bureau of STD/HIV Prevention at (573) 751-6141.

Additional information for medical providers on STDs and STD training courses is available on the Internet at the following sites:

CDC's Division of STD Prevention:
http://www.cdc.gov/nchstp/dstd/dstdp.html

CDC's Division of HIV/AIDS Prevention:
http://www.cdc.gov/nchstp/hiv_aids/dhap.htm

CDC's Division of AIDS, STD, and TB Laboratory Research:
http://www.cdc.gov/ncidod/dastlr/dastlr.html

National Network of STD/HIV Prevention Training Centers:
http://129.137.232.101/STDPTC.html

St. Louis STD/HIV Prevention Training Center:
http://www.umsl.edu/services/itc/std_ptc.html
Ph: (314) 747-0294 or 747-1522

Medline - National Library of Medicine:
http://igm.nlm.nih.gov/

Human Immunodeficiency Virus (HIV) Infection

Human Papillomavirus (HPV) Infection

Human Immunodeficiency Virus (HIV) Infection

DETECTION, INITIAL MANAGEMENT AND REFERRAL

Infection with HIV produces a spectrum of disease that progresses from a clinically latent or asymptomatic state to AIDS as a late manifestation. The pace of disease progression is variable. The time between infection with HIV and the development of AIDS ranges from a few months to as long as 17 years (median: 10 years). Most adults and adolescents infected with HIV remain symptom-free for long periods, but viral replication is active during all stages of infection, increasing substantially as the immune system deteriorates. AIDS eventually develops in almost all HIV-infected persons; in one study of HIV-infected adults, AIDS developed in 87% (95% confidence interval [CI]=83%–90%) within 17 years after infection. Additional cases are expected to occur among those who have remained AIDS-free for longer periods.

Greater awareness among both patients and health-care providers of the risk factors associated with HIV transmission has led to increased testing for HIV and earlier diagnosis of the infection, often before symptoms develop. The early diagnosis of HIV infection is important for several reasons. Treatments are available to slow the decline of immune system function. HIV-infected persons who have altered immune function are at increased risk for infections for which preventive measures are available (e.g., *Pneumocystis carinii* pneumonia [PCP], toxoplasmic encephalitis [TE], disseminated *Mycobacterium avium* complex [MAC] disease, tuberculosis [TB], and bacterial pneumonia). Because of its effect on the immune system, HIV affects the diagnosis, evaluation, treatment, and follow-up of many other diseases and may affect the efficacy of antimicrobial therapy for some STDs. Finally, the early diagnosis of HIV enables the health-care provider to counsel such patients and to assist in preventing HIV transmission to others.

Proper management of HIV infection involves a complex array of behavioral, psychosocial, and medical services. Although some of these services may be available in the STD treatment facility, other services, particularly medical services, are usually unavailable in this setting. Therefore, referral to a health-care provider or facility experienced in caring for HIV-infected patients is advised. Staff in STD treatment facilities should be knowledgeable about the options for referral available in their communities. While in the STD treatment facility, the HIV-infected patient should be educated about HIV infection and the various options for HIV care that are available. Because of the complexity of services required for management of HIV infection, detailed information, particularly regarding medical care, is beyond the scope of this report and may be found elsewhere (3,5,10,11). Rather, this section provides information on diagnostic testing for HIV-1 and HIV-2, counseling patients who have HIV infection, and preparing the HIV-infected patient for what to expect when medical care is necessary. Information also is provided on management of sex partners, because such services can and should be provided in the STD treatment facility before referral. Finally, the topics of HIV infection during pregnancy and in infants and children are addressed.

Diagnostic Testing for HIV-1 and HIV-2

Testing for HIV should be offered to all persons whose behavior puts them at risk for infection, including persons who seek evaluation and treatment for STDs. Counseling before and after testing (i.e., pretest and posttest counseling) is an integral part of the testing procedure (see HIV Prevention Counseling). Informed consent must be obtained before an HIV test is performed. Some states require written consent.

HIV infection usually is diagnosed by using HIV-1 antibody tests. Antibody testing begins with a sensitive screening test such as the enzyme immunoassay (EIA). Reactive screening tests must be confirmed by a supplemental test, such as the Western blot (WB) or an immunofluorescence assay (IFA). If confirmed by a supplemental test, a positive antibody test result indicates that a person is infected with HIV and is capable of transmitting the virus to others. HIV antibody is detectable in at least 95% of patients within 6 months after infection. Although a negative antibody test result usually indicates that a person is not infected, antibody tests cannot exclude infection that occurred <6 months before the test.

The prevalence of HIV-2 in the United States is extremely low, and CDC does not recommend routine testing for HIV-2 in settings other than blood centers, unless demographic or behavioral information indicates that HIV-2 infection might be present. Those at risk for HIV-2 infection include persons from a country in which HIV-2 is endemic or the sex partners of such persons. HIV-2 is endemic in parts of West Africa, and an increased prevalence of HIV-2 has been reported in Angola, France, Mozambique, and Portugal. In addition, testing for HIV-2 should be conducted when there is clinical evidence or suspicion of HIV disease in the absence of a positive test for antibodies to HIV-1 (12).

Because HIV antibody crosses the placenta, its presence in a child aged <18 months is not diagnostic of HIV infection (see Special Considerations, HIV Infection in Infants and Children).

The following are specific recommendations for diagnostic testing for HIV infection:

- Informed consent must be obtained before an HIV test is performed. Some states require written consent. (See HIV Prevention Counseling for a discussion of pretest and posttest counseling.)
- Positive screening tests for HIV antibody must be confirmed by a more specific confirmatory test (either WB or IFA) before being considered diagnostic of HIV infection.
- Patients who have positive HIV test results must either receive behavioral, psychosocial, and medical evaluation and monitoring services or be referred for these services.

Acute Retroviral Syndrome

Health-care providers should be alert for the symptoms and signs of acute retroviral syndrome, which is characterized by fever, malaise, lymphadenopathy, and skin rash. This syndrome frequently occurs in the first few weeks after HIV infection, before antibody test results become positive. Suspicion of acute retroviral syndrome should prompt nucleic acid testing to detect the presence of HIV. Recent data indicate that initiation of antiretroviral therapy during this period can delay the onset of HIV-related complications and might influence prognosis. If testing reveals acute HIV infection, health-care providers should either counsel the patient about immediate initiation of antiretroviral therapy or refer the patient for emergency expert consultation. The optimal antiretroviral regimen at this time is unknown. Treatment with zidovudine can delay the onset of HIV-related complications; however, most experts recommend treatment with two nucleoside reverse transcriptase inhibitors and a protease inhibitor.

Counseling for HIV-Infected Patients

Behavioral and psychosocial services are an integral part of health care for HIV-infected patients; such services should be available on-site or through referral when HIV infection is diagnosed. Patients often are distressed when first informed of a positive HIV test result. Such patients face several major adaptive challenges: a) accepting the possibility of a shortened life span, b) coping with others' reactions to a stigmatizing illness, c) developing and adopting strategies for maintaining physical and emotional health, and d) initiating changes in behavior to prevent HIV transmission to others. Many patients also require assistance with making reproductive choices, gaining access to health services, and confronting employment or housing discrimination.

Interrupting HIV transmission depends on behavioral changes made by those persons at risk for transmitting or acquiring infection. Infected persons, as potential sources of new infections, must receive additional counseling and assistance to support partner notification and counseling to prevent infection of others. Targeting behavior change programs toward HIV-infected persons and their sex partners, or those with whom they share injecting-drug equipment, is an important adjunct to AIDS prevention efforts.

The following are specific recommendations for counseling HIV-infected patients:

- Persons who test positive for HIV antibody should be counseled by a person or persons, either on-site or through referral, who can discuss the behavioral, psychosocial, and medical implications of HIV infection.
- Appropriate social support and psychological resources should be available, either on-site or through referral, to assist patients in coping with emotional distress.
- Persons who continue to be at risk for transmitting HIV should receive assistance in changing or avoiding behaviors that can transmit infection to others.

Planning for Medical Care and for Continuation of Psychosocial Services

Practice settings for offering HIV care differ depending on local resources and needs. Primary-care providers and outpatient facilities must ensure that appropriate resources are available for each patient and must avoid fragmentation of care as much as possible. A single source that is able to provide comprehensive care for all stages of HIV infection is preferred; however, the limited availability of such resources often results in the need to coordinate care among outpatient, inpatient, and specialist providers in different locations. Providers should do everything possible to avoid fragmentation of care and long delays between diagnosis of HIV infection and access to medical and psychosocial services.

Recently identified HIV infection may not have been recently acquired. Persons newly diagnosed with HIV may be at any of the different stages of infection. Therefore, the health-care provider should be alert for symptoms or signs that suggest advanced HIV infection (e.g., fever, weight loss, diarrhea, cough, shortness of breath, and oral candidiasis). The presence of any of these symptoms should prompt urgent referral for medical care. Similarly, the provider should be alert for signs of severe psychologic distress and be prepared to refer the client accordingly.

HIV-infected patients in the STD treatment setting should be educated about what to expect when medical care is necessary (11). In the nonemergent situation, the initial evaluation of the HIV-positive patient usually includes the following components:

- A detailed medical history, including sexual and substance-abuse history, previous STDs, and specific HIV-related symptoms or diagnoses.
- A physical examination; for women, this should include a gynecologic examination.
- For women, testing for *N. gonorrhoeae* and *C. trachomatis*, a Pap smear, and wet mount examination of vaginal secretions.
- Complete blood and platelet counts and blood chemistry profile.
- Toxoplasma antibody test, tests for hepatitis B viral markers, and syphilis serology.
- A CD4+ T-lymphocyte analysis and determination of HIV plasma ribonucleic acid (i.e., HIV viral load).
- A tuberculin skin test (TST) (sometimes referred to as a purified protein derivative [PPD] skin test) administered by the Mantoux method. The test result should be evaluated at 48–72 hours; in HIV-infected persons, a 5 mm induration is considered positive. The usefulness of anergy testing is controversial (13–15).
- A chest radiograph.
- A thorough psychosocial evaluation, including ascertainment of behavioral factors indicating risk for transmitting HIV and elucidation of information concerning any partners who should be notified about possible exposure to HIV.

In subsequent visits, once the results of laboratory and skin tests are available, the patient may be offered antiretroviral therapy (16), as well as specific medications to reduce the incidence of opportunistic infections (e.g., PCP, TE, disseminated MAC infection, and TB) (10,14,17–19). Hepatitis B vaccination should be offered to patients who do not have hepatitis B markers, influenza vaccination should be offered annually, and pneumococcal vaccination should be administered. For additional information concerning vaccination of HIV-infected patients, refer to "Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of Vaccines and Immune Globulins in Persons with Altered Immunocompetence" (20).

Specific recommendations for planning medical care and continuation of psychosocial services include the following:

- HIV-infected persons should be referred for appropriate follow-up to facilities in which health-care personnel are experienced in providing care for HIV-infected patients.
- Health-care providers should be alert for medical or psychosocial conditions that require immediate attention.
- Patients should be educated about what to expect in follow-up medical care.

Management of Sex Partners and Injecting-Drug Partners

When referring to persons who are infected with HIV, the term "partner" includes not only sex partners but also injecting-drug users who share syringes or other injection equipment. The rationale for partner notification is that the early diagnosis and treatment of HIV infection possibly reduces morbidity and provides the opportunity to encourage risk-reducing behaviors. Partner notification for HIV infection must be confidential and will depend on voluntary cooperation of the patient.

Two complementary notification processes, patient referral and provider referral, can be used to identify partners. With patient referral, patients directly inform their partners of their exposure to HIV infection. With provider referral, trained health department personnel locate partners on the basis of the names, descriptions, and addresses provided by the patient. During the notification process, the anonymity of patients is protected; their names are not revealed to partners who are notified. Many state health departments provide assistance, if requested, with provider-referral partner notification.

The results of one randomized trial suggested that provider referral is more effective in notifying partners than patient referral. In that study, 50% of partners in the provider-referral group were notified, compared with 7% of partners notified by persons in the patient-referral group. However, whether behavioral change takes place as a result of partner notification has not been determined, and many patients are reluctant to disclose the names of partners because of concern about discrimination, disruption of relationships, loss of confidentiality for the partners, and possible violence.

The following are specific recommendations for implementing partner-notification procedures:

- HIV-infected patients should be encouraged to notify their partners and to refer them for counseling and testing. If requested by the patient, health-care providers should assist in this process, either directly or by referral to health department partner-notification programs.
- If patients are unwilling to notify their partners, or if they cannot ensure that their partners will seek counseling, physicians or health department personnel should use confidential procedures to notify the partners.

Special Considerations

Pregnancy

All pregnant women should be offered HIV testing as early in pregnancy as possible (21). This recommendation is particularly important because of the available treatments for reducing the likelihood of perinatal transmission and maintaining the health of the woman. HIV-infected women should be informed specifically about the risk for perinatal infection. Current evidence indicates that 15%–25% of infants born to untreated HIV-infected mothers are infected with HIV; the virus also can be transmitted from an infected mother by breastfeeding. Zidovudine (ZDV) reduces the risk for HIV transmission to the infant from approximately 25% to 8% if administered to women during the later stage of pregnancy and during labor and to infants for the first 6 weeks of life (22). Therefore, ZDV treatment should be offered to all HIV-infected pregnant women. In the United States, HIV-infected women should be advised not to breastfeed their infants.

Insufficient information is available regarding the safety of ZDV or other antiretroviral drugs during early pregnancy; however, on the basis of the ACTG-076 protocol,* ZDV is indicated for the prevention of maternal-fetal HIV transmission as part of a regimen that includes oral ZDV at 14–34 weeks of gestation, intravenous (IV) ZDV during labor, and ZDV Syrup to the neonate after birth (22). Glaxo Wellcome, Inc., Hoffmann-LaRoche, Inc., Bristol-Myers Squibb, Co., and Merck & Co., Inc., in cooperation with CDC, maintain a registry to assess the safety of ZDV, didanosine (ddI), lamivudine (3TC), saquinavir (SAQ), stavudine (d4t), and dideoxycytodine (ddC) during pregnancy. Women who receive any of these drugs during pregnancy should be reported to this registry; telephone (800) 722-9292, extension 38465. The number of cases reported through February 1997 represented a sample of insufficient size for reliably estimating the risk for birth defects after administration of ddI, 3TC, SAQ, d4t, ddC, or ZDV, or their combination, to pregnant women and their fetuses. However, the registry findings did not indicate an increase in the number of birth defects after receipt of only ZDV in comparison with the number expected in the U.S. population. Furthermore, no consistent pattern of birth defects has been observed that would suggest a common cause.

*The Acquired Immunodeficiency Syndrome (AIDS) Clinical Trials Group Protocol 076, a clinical trial sponsored by the National Institutes of Health in collaboration with the National Institute of Health and Medical Research and the National Agency of Research on AIDS in France.

Women should be counseled about their options regarding pregnancy. The objective of counseling is to provide HIV-infected women with information for making reproductive decisions, analogous to the model used in genetic counseling. In addition, contraceptive counseling should be offered to HIV-infected women who do not desire pregnancy. Prenatal and abortion services should be available on-site or by referral. Pregnancy among HIV-infected women does not appear to increase maternal morbidity or mortality.

HIV Infection in Infants and Children

HIV-infected infants and young children differ from adults and adolescents with respect to the diagnosis, clinical presentation, and management of HIV disease. For example, because of transplacental passage of maternal HIV antibody, both infected and uninfected infants born to HIV-infected mothers are expected to have positive HIV-antibody test results. A definitive determination of HIV infection in a child <18 months of age should be based on laboratory evidence of HIV in blood or tissues by culture, nucleic acid, or antigen detection. In addition, CD4+ lymphocyte counts are higher in infants and children aged <5 years than in healthy adults and must be interpreted accordingly. All infants born to HIV-infected mothers should begin PCP prophylaxis at age 4–6 weeks; such prophylaxis should be continued until HIV infection has been excluded (18). Other modifications must be made in health services that are recommended for infants and children, such as avoiding vaccination with live oral polio vaccine when a child (or household contact) is infected with HIV. Management of infants, children, and adolescents who are known or suspected to be infected with HIV requires referral to physicians familiar with the manifestations and treatment of pediatric HIV infection.

Human Papillomavirus (HPV) Infection

GENITAL WARTS

More than 20 types of HPV can infect the genital tract. Most HPV infections are asymptomatic, subclinical, or unrecognized. Visible genital warts usually are caused by HPV types 6 or 11. Other HPV types in the anogenital region (i.e., types 16, 18, 31, 33, and 35) have been strongly associated with cervical dysplasia. Diagnosis of genital warts can be confirmed by biopsy, although biopsy is rarely needed (e.g., if the diagnosis is uncertain; the lesions do not respond to standard therapy; the disease worsens during therapy; the patient is immunocompromised; or warts are pigmented, indurated, fixed, and ulcerated). No data support the use of type-specific HPV nucleic acid tests in the routine diagnosis or management of visible genital warts.

HPV types 6 and 11 also can cause warts on the uterine cervix and in the vagina, urethra, and anus; these warts are sometimes symptomatic. Intra-anal warts are seen predominately in patients who have had receptive anal intercourse; these warts are distinct from perianal warts, which can occur in men and women who do not have a history of anal sex. Other than the genital area, these HPV types have been associated with conjunctival, nasal, oral, and laryngeal warts. HPV types 6 and 11 are associated rarely with invasive squamous cell carcinoma of the external genitalia. Depending on the size and anatomic locations, genital warts can be painful, friable, and/or pruritic.

HPV types 16, 18, 31, 33, and 35 are found occasionally in visible genital warts and have been associated with external genital (i.e., vulvar, penile, and anal) squamous intraepithelial neoplasia (i.e., squamous cell carcinoma in situ, bowenoid papulosis, Erythroplasia of Queyrat, or Bowen's disease of the genitalia). These HPV types have been associated with vaginal, anal, and cervical intraepithelial dysplasia and squamous cell carcinoma. Patients who have visible genital warts can be infected simultaneously with multiple HPV types.

Treatment

The primary goal of treating visible genital warts is the removal of symptomatic warts. Treatment can induce wart-free periods in most patients. Genital warts often are asymptomatic. No evidence indicates that currently available treatments eradicate or affect the natural history of HPV infection. The removal of warts may or may not decrease infectivity. If left untreated, visible genital warts may resolve on their own, remain unchanged, or increase in size or number. No evidence indicates that treatment of visible warts affects the development of cervical cancer.

Regimens

Treatment of genital warts should be guided by the preference of the patient, the available resources, and the experience of the health-care provider. None of the available treatments is superior to other treatments, and no single treatment is ideal for all patients or all warts.

The available treatments for visible genital warts are patient-applied therapies (i.e., podofilox and imiquimod) and provider-administered therapies (i.e., cryotherapy, podophyllin resin, trichloroacetic acid [TCA], bichloroacetic acid [BCA], interferon, and surgery). Most patients have from one to 10 genital warts, with a total wart area of 0.5–1.0 cm^2, that are responsive to most treatment modalities. Factors that might influence selection of treatment include wart size, wart number, anatomic site of wart, wart morphology, patient preference, cost of treatment, convenience, adverse effects, and provider experience. Having a treatment plan or protocol is important, because many patients will require a course of therapy rather than a single treatment. In general, warts located on moist surfaces and/or in intertriginous areas respond better to topical treatment (e.g., TCA, podophyllin, podofilox, and imiquimod) than do warts on drier surfaces.

The treatment modality should be changed if a patient has not improved substantially after three provider-administered treatments or if warts have not completely cleared after six treatments. The risk-benefit ratio of treatment should be evaluated throughout the course of therapy to avoid overtreatment. Providers should be knowledgeable about, and have available to them, at least one patient-applied and one provider-administered treatment.

Complications rarely occur if treatments for warts are employed properly. Patients should be warned that scarring in the form of persistent hypopigmentation or hyperpigmentation is common with ablative modalities. Depressed or hypertrophic scars are rare but can occur, especially if the patient has had insufficient time to heal between treatments. Treatment can result rarely in disabling chronic pain syndromes (e.g., vulvodynia or hyperesthesia of the treatment site).

External Genital Warts, Recommended Treatments

Patient-Applied:

Podofilox 0.5% solution or gel. Patients may apply podofilox solution with a cotton swab, or podofilox gel with a finger, to visible genital warts twice a day for 3 days, followed by 4 days of no therapy. This cycle may be repeated as necessary for a total of four cycles. The total wart area treated should not exceed 10 cm^2, and a total volume of podofilox should not exceed 0.5 mL per day. If possible, the health-care provider should apply the initial treatment to demonstrate the proper application technique and identify which warts should be treated. *The safety of podofilox during pregnancy has not been established.*

OR

Imiquimod 5% cream. Patients should apply imiquimod cream with a finger at bedtime, three times a week for as long as 16 weeks. The treatment area should be washed with mild soap and water 6–10 hours after the application. Many patients may be clear of warts by 8–10 weeks or sooner. *The safety of imiquimod during pregnancy has not been established.*

Provider-Administered:

Cryotherapy with liquid nitrogen or cryoprobe. Repeat applications every 1 to 2 weeks.

OR

Podophyllin resin 10%–25% in compound tincture of benzoin. A small amount should be applied to each wart and allowed to air dry. To avoid the possibility of complications associated with systemic absorption and toxicity, some experts recommend that application be limited to ≤0.5 mL of podophyllin or ≤10 cm^2 of warts per session. Some experts suggest that the preparation should be thoroughly washed off 1–4 hours after application to reduce local irritation. Repeat weekly if necessary. *The safety of podophyllin during pregnancy has not been established.*

OR

TCA or BCA 80%–90%. Apply a small amount only to warts and allow to dry, at which time a white "frosting" develops; powder with talc or sodium bicarbonate (i.e., baking soda) to remove unreacted acid if an excess amount is applied. Repeat weekly if necessary.

OR

Surgical removal either by tangential scissor excision, tangential shave excision, curettage, or electrosurgery.

External Genital Warts, Alternative Treatments

Intralesional interferon,

OR

Laser surgery.

For patient-applied treatments, patients must be able to identify and reach warts to be treated. Podofilox 0.5% solution or gel is relatively inexpensive, easy to use, safe, and self-applied by patients. Podofilox is an antimitotic drug that results in destruction of warts. Most patients experience mild/moderate pain or local irritation after treatment. Imiquimod is a topically active immune enhancer that stimulates production of interferon and other cytokines. Before wart resolution, local inflammatory reactions are common; these reactions usually are mild to moderate.

Cryotherapy, which requires the use of basic equipment, destroys warts by thermal-induced cytolysis. Its major drawback is that proper use requires substantial training, without which warts are frequently overtreated or undertreated, resulting in poor efficacy or increased likelihood of complications. Pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, are not unusual. Although local anesthesia (topical or injected) is not used routinely, its use facilitates treatment if there are many warts or if the area of warts is large.

Podophyllin resin contains a number of compounds, including the podophyllin lignans that are antimitotic. The resin is most frequently compounded at 10%–25% in tincture of benzoin. However, podophyllin resin preparations differ in the concentration of active components and contaminants. The shelf life and stability of podophyllin preparations are unknown. It is important to apply a thin layer of podophyllin resin to the warts and allow it to air dry before the treated area comes into contact with clothing. Overapplication or failure to air dry can result in local irritation caused by spread of the compound to adjacent areas.

Both TCA and BCA are caustic agents that destroy warts by chemical coagulation of the proteins. Although these preparations are widely used, they have not been investigated thoroughly. TCA solutions have a low viscosity comparable to water and can spread rapidly if applied excessively, thus damaging adjacent normal tissue. Both TCA and BCA should be applied sparingly and allowed to dry before the patient sits or stands. If pain is intense, the acid can be neutralized with soap or sodium bicarbonate (i.e., baking soda).

Surgical removal of warts has an advantage over other treatment modalities in that it renders the patient wart-free, usually with a single visit. However, substantial clinical training, additional equipment, and a longer office visit are required. Once local anesthesia is achieved, the visible genital warts can be physically destroyed by electrosurgery, in which case no additional hemostasis is required. Alternatively, the warts can be removed either by tangential excision with a pair of fine scissors or a scalpel or by curettage. Because most warts are exophytic, this can be accomplished with a resulting wound that only extends into the upper dermis. Hemostasis can be achieved with an electrosurgical unit or a chemical styptic (e.g., an aluminum chloride solution). Suturing is neither required nor indicated in most cases when surgical removal is done properly. Surgery is most beneficial for patients who have a large number or area of genital warts. Carbon dioxide laser and surgery may be useful in the management of extensive warts or intraurethral warts, particularly for those patients who have not responded to other treatments.

Interferons, either natural or recombinant, used for the treatment of genital warts have been administered systemically (i.e., subcutaneously at a distant site or IM) and intralesionally (i.e., injected into the warts). Systemic interferon is not effective. The efficacy and recurrence rates of intralesional interferon are comparable to other treatment modalities. Interferon is believed to be effective because of antiviral and/or immunostimulating effects. However, interferon therapy is not recommended for routine use because of inconvenient routes of administration, frequent office visits, and the association between its use and a high frequency of systemic adverse effects.

Because of the shortcomings of available treatments, some clinics employ combination therapy (i.e., the simultaneous use of two or more modalities on the same wart at the same time). Most experts believe that combining modalities does not increase efficacy but may increase complications.

Cervical Warts

For women who have exophytic cervical warts, high-grade squamous intraepithelial lesions (SIL) must be excluded before treatment is begun. Management of exophytic cervical warts should include consultation with an expert.

Vaginal Warts

Cryotherapy with liquid nitrogen. The use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation.

OR

TCA or BCA 80%–90% applied only to warts. Apply a small amount only to warts and allow to dry, at which time a white "frosting" develops; powder with talc or sodium bicarbonate (i.e., baking soda) to remove unreacted acid if an excess amount is applied. Repeat weekly if necessary.

OR

Podophyllin 10%–25% in compound tincture of benzoin applied to a treated area that must be dry before the speculum is removed. Treat with ≤2 cm^2 per session. Repeat application at weekly intervals. Because of concern about potential systemic absorption, some experts caution against vaginal application of podophyllin. *The safety of podophyllin during pregnancy has not been established.*

Urethral Meatus Warts

Cryotherapy with liquid nitrogen,

OR

Podophyllin 10%–25% in compound tincture of benzoin. The treatment area must be dry before contact with normal mucosa. Podophyllin must be applied weekly if necessary. *The safety of podophyllin during pregnancy has not been established.*

Anal Warts

Cryotherapy with liquid nitrogen.

OR

TCA or BCA 80%–90% applied to warts. Apply a small amount only to warts and allow to dry, at which time a white "frosting" develops; powder with talc or sodium bicarbonate (i.e., baking soda) to remove unreacted acid if an excess amount is applied. Repeat weekly if necessary.

OR

Surgical removal.

Note: Management of warts on rectal mucosa should be referred to an expert.

Oral Warts

Cryotherapy with liquid nitrogen,

OR

Surgical removal.

Follow-Up

After visible genital warts have cleared, a follow-up evaluation is not mandatory. Patients should be cautioned to watch for recurrences, which occur most frequently during the first 3 months. Because the sensitivity and specificity of self-diagnosis of genital warts is unknown, patients concerned about recurrences should be offered a follow-up evaluation 3 months after treatment. Earlier follow-up visits also may be useful a) to document a wart-free state, b) to monitor for or treat complications of therapy, and c) to provide the opportunity for patient education and counseling. Women should be counseled regarding the need for regular cytologic screening as recommended for women without genital warts. The presence of genital warts is not an indication for cervical colposcopy.

Management of Sex Partners

Examination of sex partners is not necessary for the management of genital warts because the role of reinfection is probably minimal and, in the absence of curative therapy, treatment to reduce transmission is not realistic. However, because self- or partner-examination has not been evaluated as a diagnostic method for genital warts, sex partners of patients who have genital warts may benefit from examination to assess the presence of genital warts and other STDs. Sex partners also might benefit from counseling about the implications of having a partner who has genital warts. Because treatment of genital warts probably does not eliminate the HPV infection, patients and sex partners should be cautioned that the patient might remain infectious even though the warts are gone. The use of condoms

may reduce, but does not eliminate, the risk for transmission to uninfected partners. Female sex partners of patients who have genital warts should be reminded that cytologic screening for cervical cancer is recommended for all sexually active women.

Special Considerations

Pregnancy

Imiquimod, podophyllin, and podofilox should not be used during pregnancy. Because genital warts can proliferate and become friable during pregnancy, many experts advocate their removal during pregnancy. HPV types 6 and 11 can cause laryngeal papillomatosis in infants and children. The route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood. The preventive value of cesarean section is unknown; thus, cesarean delivery should not be performed solely to prevent transmission of HPV infection to the newborn. In rare instances, cesarean delivery may be indicated for women with genital warts if the pelvic outlet is obstructed or if vaginal delivery would result in excessive bleeding.

Immunosuppressed Patients

Persons who are immunosuppressed because of HIV or other reasons may not respond as well as immunocompetent persons to therapy for genital warts, and they may have more frequent recurrences after treatment. Squamous cell carcinomas arising in or resembling genital warts might occur more frequently among immunosuppressed persons, requiring more frequent biopsy for confirmation of diagnosis.

Squamous Cell Carcinoma in situ

Patients in whom squamous cell carcinoma in situ of the genitalia is diagnosed should be referred to an expert for treatment. Ablative modalities usually are effective, but careful follow-up is important. The risk for these lesions leading to invasive squamous cell carcinoma of the external genitalia in immunocompetent patients is unknown but is probably low. Female partners of patients who have squamous cell carcinoma in situ are at high risk for cervical abnormalities.

SUBCLINICAL GENITAL HPV INFECTION (WITHOUT EXOPHYTIC WARTS)

Subclinical genital HPV infection occurs more frequently than visible genital warts among both men and women. Infection often is indirectly diagnosed on the cervix by Pap smear, colposcopy, or biopsy and on the penis, vulva, and other genital skin by the appearance of white areas after application of acetic acid. However, the routine use of acetic acid soaks and examination with light and magnification, as a screening test, to detect “subclinical” or “acetowhite” genital warts is not recommended. Acetowhitening is not a specific test for HPV infection. Thus, in populations at low risk for this infection, many false-positives may be detected when this test is used for screening. The specificity and sensitivity of this procedure has not been defined. In special situations, experienced clinicians find this test useful for identification of flat genital warts.

A definitive diagnosis of HPV infection depends on detection of viral nucleic acid (DNA or RNA) or capsid protein. Pap smear diagnosis of HPV does not always correlate with detection of HPV DNA in cervical cells. Cell changes attributed to HPV in the cervix are similar to those of mild dysplasia and often regress spontaneously without treatment. Tests that detect several types of HPV DNA or RNA in cells scraped from the cervix are available, but the clinical utility of these tests for managing patients is unclear. Management decisions should not be made on the basis of HPV tests. Screening for subclinical genital HPV infection using DNA or RNA tests or acetic acid is not recommended.

Treatment

In the absence of coexistent dysplasia, treatment is not recommended for subclinical genital HPV infection diagnosed by Pap smear, colposcopy, biopsy, acetic acid soaking of genital skin or mucous membranes, or the detection of HPV (DNA or RNA). The diagnosis of subclinical genital HPV infection is often questionable, and no therapy has been identified to eradicate infection. HPV has been demonstrated in adjacent tissue after laser treatment of HPV-associated dysplasia and after attempts to eliminate subclinical HPV by extensive laser vaporization of the anogenital area. In the presence of coexistent dysplasia, management should be based on the grade of dysplasia.

Management of Sex Partners

Examination of sex partners is unnecessary. Most sex partners of infected patients probably are already infected subclinically with HPV. No practical screening tests for subclinical infection are available. The use of condoms may reduce transmission to sex partners who are likely to be uninfected (e.g., new partners); however, the period of communicability is unknown. Whether patients who have subclinical HPV infection are as contagious as patients who have exophytic warts is unknown.

Medical providers play a vital role in the prevention and control of sexually transmitted diseases (STDs). Providers can help significantly reduce the occurrence of these diseases by:

- Evaluating each patient, as appropriate, for evidence of STDs, and for evidence of high-risk sexual behaviors.
- Promptly diagnosing and treating patients with STDs according to current guidelines.
- Providing appropriate follow-up after patients have been treated.
- Providing education and counseling to patients engaging in high-risk sexual behaviors.
- Promptly reporting, as required by Missouri law, all cases of chlamydial infection, gonorrhea, syphilis, and hepatitis B to the local health department, or to the Missouri Department of Health (DOH) at (573) 751-6463. Reports of cases of HIV infection/AIDS should be made as follows:
  - Health care providers in St. Louis City and St. Louis County should report the individual to the St. Louis City Department of Health and Hospitals at (314) 658-1159.
  - Providers in the five-county Kansas City metropolitan area should report to the Kansas City Health Department at (816) 983-4200.
  - All other providers should report to DOH's Office of Surveillance at (573) 751-6463.

CORRECTIONS/ADDITIONS

The following corrections/additions should be noted relative to the May-June 1998 issue of the *Missouri Epidemiologist*:

- Table 1 on page 4—The *Staphylococcus aureus* outbreak in a restaurant should have been listed as foodborne.
- Table 2 on page 5—The Legionellosis outbreak should have been listed as airborne. Epidemiologic evidence supports airborne transmission via aerosol-producing devices; other modes are possible, but none has been proven conclusively. Person-to-person transmission has not been documented.
- Sidebar on page 29—The federal government has released updated guidelines for treatment of HIV disease in adults and adolescents. "Guidelines for the Use of Antiretroviral Agents in HIV-infected adults and adolescents (June 17, 1998)" can be found at **http://www.hivatis.org/trtgdlns.html**. The International AIDS Society–USA Panel also released updated recommendations for treatment of HIV disease. "Antiretroviral Therapy for HIV Infection in 1998" can be found at **http://www.ama-assn.org/sci-pubs/journals/archive/jama/vol_280/no_1/jst80004.htm**.
- Table 1 on page 9 contained some errors. We have reprinted a corrected version below.

Table 1. Reporting Criteria for Tick-Borne Diseases
(A confirmed case meets both clinical and laboratory criteria.)

	Ehrlichiosis	Tularemia	Rocky Mountain Spotted Fever	Borelliosis*
Clinical	Tick exposure, acute onset, febrile myalgia, headache, rigor, malaise	Several disease forms, ulceroglandular, intestinal, pneumonic	Tick exposure, acute onset, febrile, myalgia, headache, petichial rash	Characteristic erythematous rash >5 cm in diameter **OR** Chronic manifestations
AND				
Laboratory	Four-fold titer rise in IFA for *E. canis* or *E. chaffeensis* **or** PCR **or** *Intracytoplasmic morulae* + IFA >64	Isolate *F. tularensis* **or** four-fold titer rise for *F. tularensis* antigen	Four-fold titer rise in IFA for *Rickettsia rickettsii* **or** PCR **or** isolate	Isolation of *B. burgdorferi* **or** EIA + Blot** **or** IFA + Blot**

*Lab methods are not decisive in Missouri and are not required for confirmation.
**Blot+ is 2/5 IgM and 5/10 IgG bands

Osteoporosis Prevention and Education

Virginia Beatty
Bureau of Chronic Disease Control

Missouri physicians strive to keep current on the latest technology and treatment options available to their patients in order to ensure quality care. The Department of Health's Missouri Osteoporosis Prevention and Education Program is also dedicated to assuring quality care and keeping physicians and the general public aware of certified technologists, treatment and other information. Therefore, we want to draw your attention to an organization that is dedicated to ensuring quality densitometry screening and lab result interpretation in the diagnosis of osteoporosis. The International Society for Clinical Densitometry (ISCD) is the only organization that currently certifies physicians and technologists. It was founded in 1993 by a multi-disciplinary group of physicians and scientists to fulfill the need for a society dedicated to the practice of bone measurement.

Mission of ISCD

The ISCD is a not-for-profit medical, scientific and professional society. It links multiple disciplines through an international organization dedicated to the clinical and educational aspects of bone densitometry by:

- Enhancing greater knowledge and quality of densitometry among health care professionals,
- Providing continuing education and professional certification for physicians and technologists, and site accreditation for densitometry facilities,
- Increasing patient awareness and access to densitometry, and
- Supporting clinical and scientific advances in the osteoporosis field.

Physicians can help assure that Missourians continue to receive the highest quality of care by pursuing certification and supporting certification of technologists. Being certified brings added credibility to your office, hospital affiliation and third party payers. ISCD has several conferences scheduled in the continental United States that may be of interest to you. See sidebar. For more information, contact ISCD Headquarters, 1200 19th Street NW, Suite 300; Washington, DC 20036-2422; Ph: (202) 828-6056; FAX: (202) 857-1102; E-mail: www.iscd.org.

Osteoporosis Conference Update

ISCD Certification Program
January 14-17, 1999
New Orleans, LA

This professional certification program is a means of qualifying interpreting physicians and densitometry technologists. The program was developed based upon the requests and inquiries of state regulatory agencies, reimbursement authorities, managed care organizations and others with a special interest in the quality delivery of bone measurement services.

Physician Course Content:

- Basic science of bone densitometry
- Principles of operation of commercially available instruments
- Clinical utility of bone density testing
- Interpretation and reporting
- T-, Z-scores and World Health Organization Criteria
- Clinical decision-making using bone mineral density data

Registration:
Space is limited, so register early. To register, you may do so by visiting the website: www.iscd.org or by calling the ISCD Professional Certification and Site Accreditation Office at (503) 288-8323.

Bone Ultrasonometry 3: A Third International Symposium for Clinical Practitioners
April 15-17, 1999
Key West, Florida.

The tentative revisions for the expanded 1999 program include:

- More coverage for current clinical findings, research and oral presentations
- Longer Q&A, roundtable and discussion sessions
- Increased opportunity to "Meet the Manufacturers"
- Integration of ultrasound with other techniques
- More extensive session for basic science, *in-vitro studies* and new technical and instrumentation developments affecting clinical practice
- Clinical quality assurance
- Public health initiatives and education/awareness efforts in the clinical and patient communities
- Case studies and clinical management strategies
- Commercial exhibits

Contact:
Bone Ultrasonometry 3 at FAX: (503) 281-4545 or E-mail: certify@iscd.org.

(continued from page 14)
For purposes of considering HIV PEP, the evaluation also should include information about medications the HCW may be taking and any current or underlying medical conditions or circumstances (i.e., pregnancy, breast feeding, or renal or hepatic disease) that may influence drug selection. Pregnancy testing should be offered to all nonpregnant women of childbearing age whose pregnancy status is unknown.

HIV PEP

The following recommendations apply to situations where an HCW has had an exposure to a source-person with HIV or where information suggests that there is a likelihood that the source-person is HIV-infected. These recommendations are based on the risk for HIV infection after different types of exposure and limited data regarding efficacy and toxicity of PEP. Because most occupational HIV exposures do not result in the transmission of HIV, potential toxicity must be carefully considered when prescribing PEP. When possible, these recommendations should be implemented in consultation with persons having expertise in antiretroviral therapy and HIV transmission.

Explaining PEP to HCWs

Recommendations for chemoprophylaxis should be explained to HCWs who have sustained occupational HIV exposures (Figure 1). For exposures for which PEP is considered appropriate, HCWs should be informed that a) knowledge about the efficacy and toxicity of drugs used for PEP are limited; b) only ZDV has been shown to prevent HIV transmission in humans; c) there are no data to address whether adding other antiretroviral drugs provides any additional benefit for PEP, but experts recommend combination drug regimens because of increased potency and concerns about drug-resistant virus; d) data regarding toxicity of antiretroviral drugs in persons without HIV infection or in pregnant women are limited for ZDV and not known regarding other antiretroviral drugs; and e) any or all drugs for PEP may be declined by the HCW. HCWs who have HIV occupational exposures for which PEP is not recommended should be informed that the potential side effects and toxicity of taking PEP outweigh the negligible risk of transmission posed by the type of exposure.

Factors in Selection of a PEP Regimen

Selection of the PEP regimen should consider the comparative risk represented by the exposure and information about the exposure source, including history of and response to antiretroviral therapy based on clinical response, CD4+ T-lymphocyte counts, viral load measurements, and current disease stage. Most HIV exposures will warrant only a two-drug regimen, using two NRTIs, usually ZDV and 3TC. The addition of a third drug, usually a PI (i.e., IDV or NEL), should be considered for exposures that pose an increased risk for transmission or where resistance to the other drugs used for PEP is known or suspected.

Timing of PEP Initiation

PEP should be initiated as soon as possible. The interval within which PEP should be started for optimal efficacy is not known. Animal studies have demonstrated the importance of starting PEP within hours after an exposure (43,54,56). To assure timely access to PEP, an occupational exposure should be regarded as an urgent medical concern and PEP started as soon as possible after the exposure (i.e., within a few hours rather than days). If there is a question about which antiretroviral drugs to use, or whether to use two or three drugs, it is probably better to start ZDV and 3TC immediately than to delay PEP administration. Although animal studies suggest that PEP probably is not effective when started later than 24–36 hours postexposure (42,55,56), the interval after which there is no benefit from PEP for humans is undefined. Therefore, if appropriate for the exposure, PEP should be started even when the interval since exposure exceeds 36 hours. Initiating therapy after a longer interval (e.g., 1–2 weeks) may be considered for exposures that represent an increased risk for transmission; even if infection is not prevented, early treatment of acute HIV infection may be beneficial (69). The optimal duration of PEP is unknown. Because 4 weeks of ZDV appeared protective in HCWs (2) , PEP probably should be administered for 4 weeks, if tolerated.

PEP if Serostatus of Source Person is Unknown

If the source person's HIV serostatus is unknown at the time of exposure (including when the source is HIV negative but may have had a recent HIV exposure), use of PEP should be decided on a case-by-case basis, after considering the type of exposure and the clinical and/or epidemiologic likelihood of HIV infection in the source (Figure 1). If these considerations suggest a possibility for HIV transmission and HIV testing of the source is pending, it is reasonable to initiate a two-drug PEP regimen until laboratory results have been obtained and later modify or discontinue the regimen accordingly.

PEP if Exposure Source is Unknown

If the exposure source is unknown, use of PEP should be decided on a case-by-case basis. Consideration should include the severity of the exposure and the epidemiologic likelihood that the HCW was exposed to HIV.

PEP for Pregnant HCWs

If the HCW is pregnant, the evaluation of risk and need for PEP should be approached as with any other HCW who has had an HIV exposure. However, the decision to use any antiretroviral drug during pregnancy should involve discussion between the woman and her health-care provider regarding the potential benefits and potential risks to her and her fetus.

(continued on page 28)

(continued from page 27)

Follow-up of HCWs Exposed to HIV

Postexposure Testing

HCWs with occupational exposure to HIV should receive follow-up counseling, postexposure testing, and medical evaluation regardless of whether they receive PEP. HIV-antibody testing should be performed for at least 6 months postexposure (e.g., at 6 weeks, 12 weeks, and 6 months). It is unclear whether an extended follow-up period (e.g., 12 months) is indicated in certain circumstances. Although rare instances of delayed HIV seroconversion have been reported (36,37, J.L. Gerberding, San Francisco General Hospital, unpublished data, May 1997), the infrequency of this occurrence does not warrant adding to HCWs' anxiety by routinely extending the duration of postexposure follow-up. Circumstances for which extending the duration of follow-up have been suggested include the use of highly potent antiretroviral regimens (i.e., more than two drugs) because of theoretical concerns that HIV seroconversion could be delayed, or simultaneous exposure to HCV. Data are insufficient for making a general recommendation in these situations. However, this should not preclude a decision to extend follow-up in an individual situation based on the clinical judgement of the HCW's health-care provider. HIV testing should be performed on any HCW who has an illness that is compatible with an acute retroviral syndrome, regardless of the interval since exposure. HIV-antibody testing using EIA should be used to monitor for seroconversion. The routine use of direct virus assays (e.g., HIV p24 antigen EIA or polymerase chain reaction for HIV RNA) to detect infection in exposed HCWs generally is not recommended (34). Although direct virus assays may detect HIV infection a few days earlier than EIA, the infrequency of HCW seroconversion and increased costs of these tests do not warrant their routine use in this setting. Also, HIV RNA is approved for use in established HIV infection; its reliability in detecting very early infection has not been determined.

Table 1. Basic and expanded postexposure prophylaxis regimens

Regimen category	Application	Drug regimen
Basic	Occupational HIV exposures for which there is a recognized transmission risk (Figure 1).	4 weeks (28 days) of both zidovudine 600 mg every day in divided doses (i.e., 300 mg twice a day, 200 mg three times a day, or 100 mg every 4 hours) **and** lamivudine 150 mg twice a day.
Expanded	Occupational HIV exposures that pose an increased risk for transmission (e.g., larger volume of blood and/or higher virus titer in blood) (Figure 1).	Basic regimen plus **either** indinavir 800 mg every 8 hours **or** nelfinavir 750 mg three times a day.*

*Indinavir should be taken on an empty stomach (i.e., without food or with a light meal) and with increased fluid consumption (i.e., drinking six 8 oz glasses of water throughout the day); nelfinavir should be taken with meals.

Monitoring and Management of PEP Toxicity

If PEP is used, drug-toxicity monitoring should be performed at baseline and again 2 weeks after starting PEP. Clinical judgement, based on medical conditions that may exist in the HCW and any toxicity associated with drugs included in the PEP regimen, should determine the scope of testing. Minimally these should include a complete blood count and renal and hepatic chemical function tests. Monitoring for evidence of hyperglycemia should be included for HCWs whose regimen includes any PI; if the HCW is receiving IDV, monitoring for crystalluria, hematuria, hemolytic anemia, and hepatitis also should be included. If toxicity is noted, modification of the regimen should be considered after expert consultation; further diagnostic studies may be indicated.

HCWs who fail to complete the recommended regimen often do so because of the side effects they experience (e.g., nausea and diarrhea). These symptoms often can be managed without changing the regimen by prescribing antimotility and antiemetic agents or other medications that target the specific symptoms. In other situations, modifying the dose interval (i.e., administering a lower dose of drug more frequently throughout the day, as recommended by the manufacturer), may help promote adherence to the regimen.

Counseling and Education

Although HIV infection following an occupational exposure occurs infrequently, the emotional impact of the exposure often is substantial (102,103). In addition, HCWs are given seemingly conflicting information. Although HCWs are told that there is a low risk for HIV transmission, a 4-week regimen of PEP is recommended and they are asked to commit to behavioral measures (i.e., sexual abstinence or condom use) to prevent secondary transmission, all of which influence their lives for several weeks to months (102). Therefore, access to persons who are knowledgeable about occupational HIV transmission and who can deal with the many concerns an HIV exposure may raise for the HCW is an important element of postexposure management.

HIV-exposed HCWs should be advised to use the following measures to prevent secondary transmission during the follow-up period, especially during the first 6–12 weeks after the exposure when most HIV-infected persons are expected to seroconvert: use sexual abstinence or condoms to prevent sexual transmission and to avoid pregnancy; and refrain from donating blood, plasma, organs, tissue, or semen. If the exposed HCW is breastfeeding, she should be counseled about the risk for HIV transmission through breast milk, and discontinuation of breastfeeding should be considered, especially following high-risk exposures. If the HCW chooses to receive PEP, temporary discontinuation of breastfeeding while she is taking PEP should be considered to avoid exposing

the infant to these agents. NRTIs are known to pass into breast milk; it is not known whether this also is true for PIs.

There is no need to modify a HCW's patient-care responsibilities to prevent transmission to patients based solely on an HIV exposure. If HIV seroconversion is detected, the HCW should be evaluated according to published recommendations for HIV-infected HCWs (104).

Exposed HCWs should be advised to seek medical evaluation for any acute illness that occurs during the follow-up period. Such an illness, particularly if characterized by fever, rash, myalgia, fatigue, malaise, or lymphadenopathy, may be indicative of acute HIV infection but also may be due to a drug reaction or another medical condition.

Exposed HCWs who choose to take PEP should be advised of the importance of completing the prescribed regimen. Information should be provided about potential drug interactions and the drugs that should not be taken with PEP, the side effects of the drugs that have been prescribed (See Appendix), measures to minimize these effects, and the methods of clinical monitoring for toxicity during the follow-up period. They should be advised that the evaluation of certain symptoms should not be delayed (e.g., back or abdominal pain, pain on urination or blood in the urine, or symptoms of hyperglycemia [i.e., increased thirst and/or frequent urination]).

RECOMMENDATIONS FOR THE SELECTION OF DRUGS FOR PEP

The selection of a drug regimen for HIV PEP must strive to balance the risk for infection against the potential toxicity of the agent(s) used. Because PEP is potentially toxic, its use is not justified for exposures that pose a negligible risk for transmission (Figure 1). Also, there is insufficient evidence to recommend a highly active regimen for all HIV exposures. Therefore, two regimens for PEP are provided (Table 1): a "basic"

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STATE PUBLIC HEALTH LABORATORY REPORT

Newborn Screening — Hypothyroidism, Phenylketonuria, Galactosemia and Hemoglobinopathies

James Baumgartner, B.S., M.B.A., Chief, Metabolic Disease Unit

	Mar 98	Apr 98	Total YTD
Specimens Tested	8,791	7,818	32,768
Initial (percent)	78.0%	78.4%	25,264
Repeat (percent)	22.0%	21.6%	7,504
Specimens: Unsatisfactory	92	82	346
HT Borderline	662	700	2,932
HT Presumptive	21	17	71
PKU Borderline	1	1	3
PKU Presumptive Positive	1	1	4
GAL Borderline	5	0	10
GAL Presumptive Positive	4	2	7
FAS (Sickle cell trait)	66	77	316
FAC (Hb C trait)	27	23	99
FAE (Hb E trait)	3	1	7
FAX (Hb variant)	16	12	51
FS (Sickle cell disease)	4	4	17
FSC (Sickle C disease)	1	0	4
FC (Hb C disease)	0	1	1

	May 98	Jun 98	Total YTD
Specimens Tested	7,856	8,722	49,346
Initial (percent)	79.4%	78.3%	38,328
Repeat (percent)	20.6%	21.7%	11,018
Specimens: Unsatisfactory	105	73	524
HT Borderline	800	654	4,386
HT Presumptive	17	15	103
PKU Borderline	0	0	3
PKU Presumptive Positive	1	0	5
GAL Borderline	5	7	22
GAL Presumptive Positive	2	2	11
FAS (Sickle cell trait)	63	82	461
FAC (Hb C trait)	25	16	140
FAE (Hb E trait)	1	1	9
FAX (Hb variant)	12	12	75
FS (Sickle cell disease)	0	4	21
FSC (Sickle C disease)	2	3	9
FC (Hb C disease)	0	0	1

HT = Hypothyroidism, PKU = Phenylketonuria, GAL = Galactosemia, Hb = Hemoglobin, YTD = Year to Date

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two-drug regimen that should be appropriate for most HIV exposures and an "expanded" three-drug regimen that should be used for exposures that pose an increased risk for transmission (Figure 1) or where resistance to one or more antiretroviral agents is known or suspected. When possible, the regimens should be implemented in consultation with persons having expertise in antiretroviral treatment and HIV transmission.

Situations That Require Special Consideration

Resistance of the Source Virus to Antiretroviral Drugs

It is unknown whether drug resistance influences transmission risk; however, transmission of drug-resistant HIV has been reported (81,82) and is therefore a theoretical concern when choosing PEP regimens. If the source-person's virus is known or suspected to be resistant to one or more of the drugs included in the PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended (69). If the resistance is to one class of antiretroviral drugs, the addition to the basic PEP regimen of a drug from another class might be considered (e.g., addition of a PI when a source patient has not been treated with a PI but has virus resistant to one or more NRTIs). It is strongly recommended that PEP be started regardless of the resistance status in the source virus; if resistance is known or suspected, a third or fourth drug may be added to the regimen until consultation with a clinical expert in the treatment of HIV infection or disease can be obtained.

Known or Suspected Pregnancy in the HCW

Pregnancy should not preclude the use of optimal PEP regimens, and PEP should not be denied to a HCW solely on the basis of pregnancy. However, as discussed previously, an occupationally exposed pregnant HCW must be provided with full information about what is known and not known regarding the potential benefits and risks associated with use of the antiretroviral drugs to her and her fetus for her to make an informed decision regarding the use of PEP. The choice of antiretroviral drugs to use for PEP in pregnant HCWs is complicated by the potential need to alter dosing because of physiologic changes associated with pregnancy and the potential for short- or long-term effects on the fetus and newborn. Thus, considerations that should be discussed with a pregnant HCW include the potential risk for HIV transmission based on the type of exposure; the stage of pregnancy (the first trimester being the period of maximal organogenesis and risk for teratogenesis); and what is known about the pharmacokinetics, safety, and tolerability of the drug or combination of drugs in pregnancy.

Table 2. HIV postexposure prophylaxis resources and registries

Resource or registry	Contact information
National Clinicians' Postexposure Hotline	Telephone: (888) 448-4911
HIV Postexposure Prophylaxis Registry	Telephone: (888) 737-4448 ([888] PEP4HIV) Write: 1410 Commonwealth Drive Suite 215 Wilmington, NC 28405
Antiretroviral Pregnancy Registry	Telephone: (800) 258-4263 Fax: (800) 800-1052 Write: 1410 Commonwealth Drive Suite 215 Wilmington, NC 28405
Food and Drug Administration (for reporting unusual or severe toxicity to antiretroviral agents	Telephone: (800) 332-1088
CDC (for reporting HIV seroconversions in health-care workers who received PEP)	Telephone: (404) 639-6425

POSTEXPOSURE REGISTRIES

Health-care providers in the United States are encouraged to enroll HCWs who receive PEP in a confidential registry developed by CDC, Glaxo Wellcome Inc., and Merck & Co., Inc., to assess toxicity; Ph: (888) 737-4448 ([888] PEP-4HIV), or write the HIV PEP Registry, 1410 Commonwealth Drive, Suite 215, Wilmington, NC 28405. Unusual or serious and unexpected toxicity from antiretroviral drugs should be reported to the manufacturer and/or FDA, Ph: (800) 332-1088.

Health-care providers also should report instances of prenatal exposure to antiretroviral agents to the Antiretroviral Pregnancy Registry. The registry is an epidemiologic project to collect observational, nonexperimental data on antiretroviral drug exposure during pregnancy to assess potential teratogenicity. Referrals should be directed to the Antiretroviral Pregnancy Registry, 1410 Commonwealth Drive, Suite 215, Wilmington, NC 28405; Ph: (800) 258-4263 or (800) 722-9292, Ext. 39437; FAX: (800) 800-1052.

A protocol has been developed to evaluate HIV seroconversion in an HCW who received PEP. These events can be reported to CDC, Ph: (404) 639-6425.

RESOURCES FOR CONSULTATION

Clinicians who seek consultation on HIV PEP for assistance in managing an occupational exposure should access local experts in HIV treatment as much as possible. In addition, the "National Clinicians' Post-Exposure Prophylaxis Hotline (PEP-Line)" has been created to assist clinicians with these issues; Ph: (888) 448-4911. Other resources and registries include the HIV Postexposure Prophylaxis Registry, the Antiretroviral Pregnancy Registry, FDA, and CDC (Table 2).

ADMINISTRATIVE CONSIDERATIONS

Effective implementation of the elements of postexposure management detailed in these recommendations may require various types of expertise. The assessment of the severity of an exposure generally requires clinical training and

experience (i.e., medical or nursing). However, the assessment of HIV infection risk and initiation of a basic PEP regimen necessitates knowledge or experience in clinical epidemiology, infection control, occupational health, or the clinical treatment of HIV. Decisions about HIV PEP are particularly complex if PIs are used or there is concern about drug-resistant virus. Thus, expert consultation when prescribing PEP is strongly encouraged. PEP protocols should list the names of readily available resources for consultation and could include policies that require infectious disease evaluation before prescribing an expanded antiretroviral regimen. However, these efforts should not delay initial implementation of PEP where it is appropriate.

References for these guidelines are available above request. Please contact the Office of Epidemiology, Missouri Department of Health, 920 Wildwood Drive, Jefferson City, MO 65109, Ph: (573) 751-6128. A full copy of the guidelines in pdf format can be found on CDC's Home Page at: **http://www.cdc.gov/epo/mmwr/mmwr_rr.html.**

Appendix

FIRST-LINE DRUGS FOR HIV POSTEXPOSURE PROPHYLAXIS (PEP)*

Nucleoside Reverse Transcriptase Inhibitors

Zidovudine (RETROVIR®; ZDV, AZT)

Dosage: 600 mg every day in divided doses (e.g., 300 mg twice a day, 200 mg three times a day, or 100 mg every four hours).
Primary toxicities and/or side effects: Neutropenia, anemia, nausea, fatigue, malaise, headache, insomnia, and asthenia.
Comments: Caution should be used if co-administered with bone marrow suppressive drugs or cytotoxic therapy.

Lamivudine (EPIVIR™; 3TC)

Dosage: 150 mg twice a day.
Primary toxicities and/or side effects: Headache, abdominal pain, diarrhea, and in rare cases, pancreatitis. Toxicity of ZDV and 3TC when used in combination is approximately equal to that of ZDV alone.

ZDV plus 3TC (COMBIVIR™)

Dosage: 1 tablet twice a day; each tablet contains 300 mg ZDV and 150 mg 3TC.
Primary toxicities and/or side effects: See above for ZDV and 3TC.
Comments: Caution should be used if co-administered with bone marrow suppressive drugs or cytotoxic therapy.

Protease Inhibitors (PIs)**

Indinavir (CRIXIVAN®; IDV)

Dosage: 800 mg every 8 hours on an empty stomach (i.e., without food or with a light meal).
Primary toxicities and/or side effects: Nephrolithiasis, crystalluria, hematuria, nausea, headache, indirect hyperbilirubinemia, elevated liver function tests (LFTs), and hyperglycemia/diabetes.
Primary drug interactions†: No PI should be co-administered with terfenadine (Seldane®), astemizole (Hismanal®), cisapride (Propulsid®), triazolam, and midazolam. Rifampin should not be administered with PIs. Cytochrome P450 metabolism inhibitors like ketoconazole may increase PI plasma concentrations; dose reduction of the PI is only indicated for indinavir. Ergot alkaloid preparations should not be used in combination with PIs. If rifabutin is used concomitantly, rifabutin dose should be reduced because of inhibition of rifabutin metabolism; with concomitant indinavir or nelfinavir use, reduce rifabutin dose by 50%.

Serum levels of PIs may be increased when multiple PIs are used in combination.
Comments: Incidence of nephrolithiasis may be reduced by consuming large quantities of water (i.e., drinking six 8 oz glasses of water [total 48 oz] throughout the day).

Nelfinavir (VIRACEPT™)

Dosage: 750 mg three times a day (with meals or a light snack).
Primary toxicities and/or side effects: Diarrhea and hyperglycemia/diabetes.
Primary drug interactions†: See above for indinavir.
Comments: Diarrhea usually can be controlled with over-the-counter antidiarrheal drugs (e.g., loperamide).

If oral contraceptives are being used, alternative or additional contraceptive measures should be used while taking nelfinavir.

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*Information included in these recommendations may not represent Food and Drug Administration (FDA) approval or approved labeling for the particular products or indications in question. Specifically, the terms “safe” and “effective” may not be synonymous with the FDA-defined legal standards for product approval.

**It is recommended that consultation with experts in the treatment of HIV infection and disease be sought when considering the inclusion of PIs or the use of alternative agents in PEP regimens.

†See package insert for other contraindications and possible drug interactions.

ANTIRETROVIRAL DRUGS USED FOR TREATMENT OF HIV INFECTION THAT MAY BE CONSIDERED FOR PEP IN SPECIAL CIRCUMSTANCES

Nucleoside Reverse Transcriptase Inhibitors

Zalcitabine (HIVID®, ddC)

Dosage: 0.75 mg every 8 hours.
Primary toxicities and/or side effects: Stomatitis and peripheral neuropathy.
Primary drug interactions*: Do not co-administer ddC with didanosine or stavudine because of the potential for enhanced peripheral neuropathy.
Comments: Peripheral neuropathy from ddC is usually after prolonged exposure.

Didanosine (VIDEX®, ddI)

Dosage: 200 mg twice a day; if body weight is <60 kg, 125 mg twice a day. Should be taken on an empty stomach.
Primary toxicities and/or side effects: Pancreatitis, peripheral neuropathy, nausea, and diarrhea.
Primary drug interactions†: Do not co-administer ddI with ddC because of the potential for enhanced peripheral neuropathy.
Comments: Peripheral neuropathy from ddI is usually after prolonged exposure.
To avoid potential drug interactions, give concomitant medications 2 hours after ddI dosing.

Stavudine (ZERIT™, d4T)

Dosage: 40 mg twice a day; if body weight is <60 kg, 30 mg twice a day.
Primary toxicities and/or side effects: Peripheral neuropathy.
Primary drug interactions†: Do not co-administer d4T with ddC because of the potential for enhanced peripheral neuropathy.
Comments: Peripheral neuropathy from d4T is usually after prolonged exposure.

Protease Inhibitors (PIs)**

Ritonavir (NORVIR™)

Dosage: 600 mg twice a day; dose escalation recommended (300 mg twice a day for 1 day, 400 mg twice a day for 2 days, 500 mg twice a day for 1 day, then 600 mg twice a day for duration of regimen).
Primary toxicities and/or side effects: Nausea, emesis, diarrhea, circumoral paresthesia, taste alteration, increased cholesterol and triglycerides, hyperglycemia/diabetes, and increased LFTs.
Primary drug interactions†: No PI should be co-administered with terfenadine (Seldane®), astemizole (Hismanal®), cisapride (Propulsid®), triazolam, or midazolam. Rifampin should not be administered with PIs. Cytochrome P450 metabolism inhibitors such as ketoconazole may increase protease inhibitor plasma concentrations. Ergot alkaloid preparations should not be used in combination with PIs. Rifabutin should not be co-administered with either saquinavir (because of reduction of saquinavir serum concentrations) or ritonavir (because of increased rifabutin concentrations). Serum levels of PIs may be increased when multiple PIs are used in combination.
Comments: Ritonavir should not be used with various antiarrhythmics and certain sedatives or hypnotics. Ritonavir also has potential interactions with certain analgesics, antibiotics, antidepressants, anti-emetics, antifungals, calcium channel blockers, and other medications.
If oral contraceptives are being used, alternative or additional contraceptive measures should be used while taking ritonavir.

Saquinavir (INVIRASE™, hard-gel formulation) (FORTOVASE™, soft-gel formulation)

Dosage: INVIRASE, 600 mg three times a day with fatty meals; FORTOVASE, 1200 mg three times a day within 2 hours of a meal. (If saquinavir is used for PEP, Fortovase should be used.)
Primary toxicities and/or side effects: Diarrhea, headache, hyperglycemia/diabetes, and increased LFTs and triglycerides.
Primary drug interactions†: See above for ritonavir.

Non-nucleoside Reverse Transcriptase Inhibitors

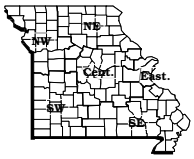
Nevirapine (VIRAMUNE®)

Dosage: 200 mg once a day for the first 2 weeks then 200 mg twice a day.
Primary toxicities and/or side effects: Rash (including rare cases of Stevens-Johnson syndrome), fever, nausea, headache, and increased LFTs.
Primary drug interactions†: Nevirapine induces hepatic cytochrome CYP3A isoforms; however, drug interaction studies with drugs metabolized by this enzyme have not been conducted. Careful monitoring is therefore recommended if nevirapine is co-administered with other drugs metabolized by this route because decreased serum concentrations (and decreased effectiveness) of the other drugs may be observed (e.g., oral contraceptives, rifampin, and rifabutin). Use of nevirapine may decrease levels of indinavir or saquinavir.
This drug should only be used in combination with other antiretroviral drugs.
Comments: Oral contraceptives may be less effective during concomitant use with nevirapine.

Delavirdine (RESCRIPTOR®)

Dosage: 400 mg three times a day
Primary toxicities and/or side effects: Rash (including rare cases of Stevens-Johnson syndrome), nausea, and increased LFTs.
Primary drug interactions†: Delavirdine inhibits hepatic cytochrome CYP3A isoforms. Should not be co-administered with terfenadine (Seldane®), astemizole (Hismanal®), cisapride (Propulsid®), triazolam, midazolam, nifedipine, anticonvulsants, amphetamines, rifabutin, or rifampin. Delavirdine may increase PI levels.
This drug should only be used in combination with other antiretroviral drugs.
Comments: Antacids and ddI decrease absorption of delavirdine and should be taken 2 hours apart.

** It is recommended that consultation with experts in the treatment of HIV infection and disease be sought when considering the inclusion of PIs or the use of alternative agents in PEP regimens.
† See package insert for other contraindications and possible drug interactions.



Missouri Department of Health
Division of Environmental Health and Communicable Disease Prevention

QUARTERLY DISEASE REPORT

Reporting Period*
January - March 1998

	Districts											3 Month State Totals		Cumulative		
	CD	** ED	NE	** NW	SE	** SW	*** OTHER	Kansas City	St. Louis City	St. Louis Co.	Spfd. Greene Co.	1997	1998	For 1997	For 1998	5 YR MEDIAN
Vaccine Preventable																
Influenza	154	139	50	11	88	66	0	5	77	387	84	41	1061	227	1061	184
Mumps	0	0	0	0	0	1	0	0	0	0	0	0	1	0	3	7
Pertussis	0	2	0	1	0	1	0	0	1	4	0	13	9	25	17	10
Measles	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Viral Hepatitis																
A	6	3	1	89	16	16	0	2	3	7	35	287	178	537	178	256
B	1	3	0	15	7	6	0	5	21	5	2	77	65	191	65	134
C	0	0	0	4	1	1	0	9	1	0	1	1	17	2	17	N/A
Non-A Non-B	0	0	1	0	0	0	0	0	0	0	0	1	1	2	1	5
Unspecified	0	0	2	0	0	0	0	0	0	0	0	1	2	1	2	N/A
Meningitis																
Aseptic Meningitis	0	1	0	5	0	0	0	2	0	5	0	15	13	27	13	26
Meningococcal Disease	0	1	0	2	2	3	0	0	0	2	1	10	11	29	11	21
Meningococcal Other	1	3	2	2	0	1	0	2	5	3	0	17	19	37	19	12
Enteric Infections																
E. Coli O157:H7	0	0	0	0	1	1	0	1	0	0	0	13	3	15	3	2
Campylobacter	4	3	6	5	10	9	0	3	13	11	5	160	69	238	69	101
Salmonella	5	8	2	15	4	6	0	6	8	11	3	223	68	298	68	94
Shigella	0	0	0	10	1	3	0	1	4	1	0	53	20	122	20	144
Parasitic Infections																
Cryptosporidiosis	0	1	0	0	0	0	0	0	0	1	0	2	2	7	1	N/A
Giardiasis	17	12	4	16	10	21	0	5	22	26	2	165	135	282	135	135
Respiratory Diseases																
Legionellosis	1	0	0	0	0	2	0	0	1	2	1	0	7	2	7	4
Sexually Transmitted																
AIDS	5	2	1	9	5	3	3	32	31	19	5	92	115	92	115	169
HIV	0	0	0	0	0	0	0	0	0	0	-	-	0	-	0	-
Chlamydia	261	80	66	224	187	236	0	579	702	533	-	-	2868	-	2868	-
Gonorrhea	146	30	17	43	79	81	0	290	683	306	-	-	1675	-	1675	-
Prim. & Sec. syphilis	0	0	0	0	12	0	0	2	17	3	-	-	34	-	34	-
Tuberculosis																
Positive PPD conversions	2	1	1	2	4	4	0	4	10	8	2	37	38	100	38	-
Zoonotic																
Ehrlichiosis	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	N/A
Lyme-like Disease	0	0	0	0	0	0	0	0	0	0	0	9	0	9	0	5
Rabies (Animal)	0	0	0	0	8	0	0	0	0	0	0	5	8	11	8	12
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	0	0	0	7	0	8	0	N/A
Tularemia	0	0	0	0	0	0	0	0	0	0	0	4	0	4	0	1

Outbreaks
Foodborne
Waterborne
Nosocomial
Pediculosis
Scabies
Giardia
Hepatitis A
Shigella
Other

Low Frequency Vaccine Preventable Diseases
Diphtheria
Hib Meningitis - 1
Hib other invasive - 2
Measles
Polio
Rubella
Tetanus

Low Frequency Diseases
Anthrax
Botulism
Brucellosis - 1
Chancroid
Cholera
Encephalitis
Granuloma Inguinale
Kawasaki Disease - 4
Leptospirosis
Listeria - 2
Lymphogranuloma Venereum
Plague
Psittacosis
Rabies (human)
Reye syndrome
Rheumatic fever, acute
Streptococcal Disease, Invasive, Grp A - 4
Streptococcus pneumoniae, Drug Resistant Invasive Disease
Toxic Shock Syndrome - 1
Trichinosis
Typhoid Fever

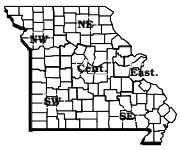
*Reporting Period Beginning January 4 and Ending March 28, 1998.
**Totals do not include Kansas City, St. Louis City, St. Louis County, or Springfield
***State and Federal Institutions
****Included in SW District
- Data unavailable

Due to data editing, totals may change

TEAR OUT FOR FUTURE REFERENCE

Missouri Morbidity and Mortality Reports of Selected Communicable Diseases - 15 Year Report

	1997	1996	1995	1994	1993	1992	1991	1990	1989	1988	1987	1986	1985	1984	1983
AIDS	501	845	769	727	1644	657	651	596	478	401	240	91	52	28	6
Brucellosis	2	2	0	0	0	0	3	1	2	4	14	4	12	7	4
Campylobacter	574	554	601	631	616	614	602	547	473	441	260	281	304	260	166
Chickenpox	6319	5830	8840	10147	9609	10009	7678	10591	9086	11350	8595	5093	2474	2565	408
Chlamydia	12257	11952	12084	12244	11625	11907	10643	11151	8151	6239	2944	1532	412	9	-
Encephalitis, Inf.	9	5	11	14	26	16	22	12	6	8	11	13	12	11	28
Giardiasis	800	777	761	774	770	739	790	878	859	654	690	516	458	462	216
Gonorrhea	7658	8415	11302	12555	13147	14887	17450	20012	21053	17241	16491	19029	20023	20042	20750
Haemophilus influenzae type B															
Meningitis	1	0	10	7	12	22	42	88	106	138	131	172	108	104	86
Other Invasive	7	8	18	44	123	59	39	57	-	-	-	-	-	-	-
Hepatitis A	1151	1414	1338	619	1443	1500	653	619	810	897	560	126	98	138	123
Hepatitis B	360	326	437	538	585	535	549	633	704	639	460	420	359	297	365
Non A, Non B	4	23	23	32	25	27	31	42	53	50	46	39	42	18	33
Unspecified	1	0	1	1	19	9	15	19	13	21	21	15	24	46	87
Influenza (confirmed)	270	283	491	163	272	111	462	220	293	148	69	78	61	39	140
Lyme Disease	28	52	53	102	108	150	207	205	108	-	-	-	-	-	-
Malaria	16	11	9	14	9	12	9	13	13	6	8	12	5	8	4
Meningitis, Aseptic	99	120	269	175	275	272	277	246	223	124	163	172	156	95	277
Meningitis, Meningococcal	43	57	54	43	34	32	37	31	21	33	35	40	46	53	55
Mumps	0	10	25	44	46	39	40	62	87	68	38	23	18	11	21
Pertussis	80	74	63	45	144	120	83	116	141	25	46	32	35	23	24
Polio, all forms	0	0	0	0	0	0	0	0	0	1	0	0	1	0	2
Rabies, Animal	31	26	30	27	35	37	28	30	62	36	59	75	59	70	96
RMSF	24	19	30	22	20	24	25	36	48	54	26	25	10	14	14
Rubella	2	0	0	2	1	1	5	3	4	0	0	1	7	0	0
Rubeola	1	3	2	161	1	0	1	103	671	65	190	32	5	6	1
Salmonellosis	568	565	577	642	529	426	616	723	676	772	660	728	690	617	602
Shigellosis	222	387	1138	654	674	742	259	284	411	607	471	89	143	244	264
Syphilis, Total	505	603	1271	1985	2499	1940	926	598	388	473	328	494	578	712	801
Primary & Secondary	118	221	584	987	1354	1167	572	272	162	154	90	110	133	186	145
Tetanus	0	1	3	1	1	1	1	0	4	1	1	2	3	6	1
Tuberculosis	248	224	244	260	256	245	254	312	278	275	339	338	311	354	399
Tularemia	18	9	25	24	17	34	44	33	39	45	58	32	35	40	51
Typhoid Fever	1	2	3	1	2	3	2	4	2	3	7	6	6	6	10
Yersinia enterocolitica	30	16	21	40	26	37	48	32	36	30	10	6	2	3	1



Missouri Department of Health
Division of Environmental Health and Communicable Disease Prevention

QUARTERLY DISEASE REPORT

Reporting Period*
April - June 1998

	Districts											3 Month State Totals		Cumulative		
	CD	** ED	NE	** NW	SE	** SW	*** OTHER	Kansas City	St. Louis City	St. Louis Co.	Spfd. Greene Co.	1997	1998	For 1997	For 1998	5 YR MEDIAN
Vaccine Preventable																
Influenza	3	0	0	4	2	0	0	1	0	3	0	41	13	227	1074	201
Mumps	0	0	0	0	0	1	0	0	0	0	0	-	1	0	1	18
Pertussis	0	2	0	1	0	0	0	0	0	0	0	12	3	25	12	24
Measles	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Viral Hepatitis																
A	5	1	1	52	15	36	0	9	2	3	45	287	169	537	347	584
B	1	2	1	10	1	9	0	6	26	4	2	77	62	191	127	242
C	0	0	0	5	0	3	0	12	0	0	1	1	21	2	38	N/A
Non-A Non-B	0	0	0	0	0	0	0	0	0	0	0	1	0	2	1	13
Unspecified	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2	N/A
Meningitis																
Aseptic Meningitis	0	15	1	3	0	0	0	0	1	19	0	15	39	27	52	63
Meningococcal Disease	0	1	1	0	0	2	0	0	0	2	2	10	8	29	19	28
Meningococcal Other	0	1	1	2	2	3	0	0	0	2	1	17	12	37	31	22
Enteric Infections																
E. Coli O157:H7	0	0	0	1	1	3	0	2	0	0	0	13	7	15	10	16
Campylobacter	13	11	10	8	18	24	0	10	3	23	20	160	140	238	209	295
Salmonella	37	15	4	27	12	13	0	10	14	30	4	223	166	298	234	250
Shigella	3	0	0	1	3	6	0	0	5	7	4	53	29	122	49	222
Parasitic Infections																
Cryptosporidiosis	0	0	1	0	0	1	0	0	2	1	1	2	6	7	8	N/A
Giardiasis	19	8	6	10	11	19	0	7	34	24	4	165	142	282	277	287
Respiratory Diseases																
Legionellosis	0	0	1	0	0	2	0	0	0	1	0	0	4	2	11	13
Sexually Transmitted																
AIDS	15	3	4	21	4	7	3	31	360	21	3	109	148	201	378	177
HIV	0	0	0	0	0	0	0	0	0	0	-	-	0	-	0	-
Chlamydia	293	73	77	254	217	239	0	547	658	483	-	2938	2843	5697	5709	-
Gonorrhea	114	21	29	92	115	52	0	676	939	421	-	2116	2459	3658	4134	-
Prim. & Sec. syphilis	0	0	0	0	2	0	0	3	13	2	-	29	23	51	54	-
Tuberculosis																
Positive PPD conversions	2	1	1	2	4	4	0	4	10	8	2	37	38	100	38	-
Zoonotic																
Ehrlichiosis	0	0	0	1	0	0	0	0	0	0	0	0	1	0	1	N/A
Lyme-like Disease	0	0	1	0	0	1	0	0	0	0	0	9	2	9	2	33
Rabies (Animal)	0	0	0	0	11	0	0	-	0	0	-	5	11	11	19	12
Rocky Mountain Spotted Fever	0	0	0	0	0	3	0	-	-	-	-	7	3	8	3	11
Tularemia	2	0	1	1	0	0	0	-	-	-	-	4	4	4	4	9

Outbreaks
Foodborne
Waterborne
Nosocomial
Pediculosis
Scabies
Giardia
Hepatitis A
Shigella
Other

Low Frequency Vaccine Preventable Diseases
Diphtheria
Hib Meningitis
Hib other invasive - 7
Measles
Polio
Rubella
Tetanus

Low Frequency Diseases
Anthrax
Botulism
Brucellosis
Chancroid
Cholera
Encephalitis - 2
Granuloma Inguinale
Kawasaki Disease - 5
Leptospirosis - 1
Listeria - 7
Lymphogranuloma Venereum
Plague
Psittacosis
Rabies (human)
Reye syndrome
Rheumatic fever, acute
Streptococcal Disease, Invasive, Grp A - 5
Streptococcus pneumoniae, Drug Resistant Invasive Disease
Toxic Shock Syndrome - 4
Trichinosis
Typhoid Fever - 1

*Reporting Period Beginning March 29 and Ending June 27, 1998.
**Totals do not include Kansas City, St. Louis City, St. Louis County, or Springfield
***State and Federal Institutions
**** Included in SW District
- Data unavailable

Due to data editing, totals may change

TEAR OUT FOR FUTURE REFERENCE

Select Communicable Diseases
Total Number of Cases Per Year
1998 Year to Date as of September 28, 1998

DISEASE	1998-YTD	1997	1996	1995	1994	1993
Influenza	1075	270	283	491	163	272
Mumps	0	0	10	25	44	46
Pertussis	0	80	74	63	0	0
Hepatitis A	487	1151	1414	1338	619	1443
Hepatitis B	167	360	326	437	538	585
Hepatitis C	77	6	-	-	-	-
Hepatitis Non-A Non-B	1	4	23	23	32	25
Hepatitis Unspecified	2	1	0	1	1	19
Meningitis	27	43	57	54	43	34
Meningitis Other	35	63	41	22	35	0
E. coli O157:H7	33	58	74	48	40	35
Campylobacter	363	574	554	601	631	616
Salmonella	447	568	424	577	642	529
Shigella	81	222	387	1138	654	674
Cryptosporidiosis	16	38	35	31	-	-
Giardia	502	800	777	761	774	770
Legionellosis	20	26	18	19	41	33
Ehrlichiosis	11	20	12	0	0	0
Lyme	2	28	52	53	102	108
Rabies	23	31	26	30	27	35
Rocky Mountain Spotted Fever	4	24	19	30	22	20

Cases of reportable diseases and conditions should be reported promptly to your local health department, or to the Missouri Department of Health at

(800) 392-0272
(during working hours)
or
(573) 751-4674
(after hours, weekends or holidays)

The U.S. Influenza Sentinel Physician Surveillance Network

Mary E. Kliethermes, R.N., B.S.
Bureau of Communicable Disease Control

During the 1997–98 influenza season, the Centers for Disease Control and Prevention (CDC) introduced a pilot influenza project called the U.S. Influenza Sentinel Physician Surveillance Network. The program was designed as an active surveillance system to provide timely reporting of current influenza-like illness. The annual influenza season begins on week 40 and continues through week 20 of the next year. For 1998–99, that will be October 4, 1998 through May 16, 1999.

CDC defines **influenza-like illness** as fever ≥100º Fahrenheit (37.8º C) and cough or sore throat, in the absence of a known cause.

State health departments were asked to recruit physicians who would volunteer to be sentinel physicians and collect the numbers of patients, stratified by age group, that they treated each week with symptoms of influenza-like illness as well as the total number of patients they saw each week. The physicians, calling a dedicated phone number using an assigned ID code and entering the data by touch-tone phone, reported the prior week's data to CDC before noon each Tuesday during the influenza season. Physicians were given the option of faxing the data into CDC to facilitate reporting. The physicians were also asked to collect viral cultures, at least two cultures from symptomatic patients at the beginning of the influenza season, two in the middle or at the peak of the season, and two during the decline of the season.

The Missouri Department of Health (DOH), Bureau of Communicable Disease Control, attempted to recruit 20 physicians to reflect a ratio of one physician for every 250,000 persons in the state. DOH was able to recruit 12 physicians and 75 percent of those physicians actively participated in the surveillance network with timely, weekly submission of data.

The Missouri State Public Health Laboratory (SPHL) shipped each participating physician a supply of virus culture kits with instructions on proper collection, storage and shipping methods. The SPHL replaced the culture kits as the physicians submitted specimens for testing. The SPHL Virology Unit processed 322 influenza cultures in 1997. The influenza sentinel physicians contributed approximately 57 of those specimens. Of the 322 cultures, 106 (33%) specimens were positive for influenza.

CDC collected the data submitted by all participating state health departments and published the influenza-like illness numbers and trends in the weekly influenza summary published each week during the influenza season and sent to state health departments. Missouri data were also available through the CDC influenza internet site, using a protected password.

CDC was very pleased with the success of the U.S. Influenza Sentinel Physician Surveillance Network pilot project and will be expanding the program for the 1998/99 influenza season. According to CDC, an influenza sentinel physician surveillance program can contribute the following:

1. Provides “real time” data and information on the spread and severity of influenza illness during the season.
2. Collection of viral cultures from ill patients to identify the circulating influenza virus strains.
3. Provides information on new circulating influenza viral strains that can be used to determine the components of the vaccine for the next influenza season and as a pandemic warning.

CDC felt that the prior influenza surveillance system was not as sensitive to a pandemic warning as it could be when compared to surveillance networks in other countries. The H5N1 influenza outbreak in Hong Kong, reinforced the need to improve the surveillance program.

DOH is developing plans for the 1998/99 influenza season to expand the influenza sentinel physician surveillance network and to improve the link between the epidemiological data and viral culture results. DOH hopes to recruit many more physicians who would be interested in participating in the influenza network to expand this valuable public health program.

If you are a Missouri physician, or nurse practitioner working in collaboration with a physician, and are interested in participating in or would like more information about the U.S. Influenza Sentinel Physician Surveillance Network, please contact the Bureau of Communicable Disease Control at (573) 751-6113 or (800) 372-0272.

Disease Reporting

Cases of reportable diseases and conditions should be reported promptly to your local health department, or to the Missouri Department of Health at

(800) 392-0272
(during working hours)
or
(573) 751-4674
(after hours, weekends or holidays)

1998–99 Recommendations for the Use of Influenza Vaccine

The following is a summary of current recommendations on influenza vaccine from the Advisory Committee on Immunization Practices (ACIP). The complete ACIP statement was published in *Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports*, Prevention and Control of Influenza, May 1, 1998, Vol. 47, No. RR-6.*

Influenza vaccine is strongly recommended for any person 6 months of age or older who is at increased risk for complications of influenza. Members of high risk groups, if they become ill, are more likely than the general population to require hospitalization. The following persons are at highest risk. They and their close contacts should be targeted for organized vaccination programs.

- Persons 65 years of age and older.
- Residents of nursing homes and other chronic-care facilities that house persons of any age with chronic medical conditions.
- Adults and children with chronic disorders of the pulmonary and cardiovascular systems, including asthma.
- Adults and children who required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies or immunosuppression (including immunosuppression caused by medications).
- Children and teenagers 6 months to 18 years of age who are receiving long-term aspirin therapy and, therefore, might be at risk for developing Reye syndrome after influenza.
- Women who will be in the second/third trimester of pregnancy during the influenza season.

Groups that can transmit influenza to persons at high risk should also be immunized. These groups include:

- Physicians, nurses and other personnel in both hospital and outpatient-care settings;
- Employees of nursing homes and chronic-care facilities who have contact with residents;
- Providers of home care to persons at high risk; and
- Household members (including children) of persons in high-risk groups.

Any person who wishes to reduce the likelihood of becoming ill with influenza should receive the vaccine.

The optimal time for organized vaccination campaigns for persons in high-risk groups is usually the period from October through mid-November. In the United States, influenza activity generally peaks between late December and early March. Administering vaccine too far in advance of the influenza season should be avoided, especially for nursing home residents, because antibody levels may begin to decline within a few months of vaccination.

Influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine. Flu vaccine contains only noninfectious viruses, and cannot cause influenza. Respiratory disease after vaccination represents coincidental illness unrelated to influenza vaccination. The most frequent side effect of vaccination, reported by fewer than one third of vaccinees, is soreness at the injection site. Unlike the 1976 swine influenza vaccine, subsequent vaccines prepared from other virus strains have not been clearly associated with an increased frequency of Guillain-Barré syndrome.

The trivalent influenza vaccine prepared for the 1998–99 season will include A/Beijing/262/95-like (H1N1), A/Sydney/5/97-like (H3N2), and B/Beijing/184/93-like hemagglutinin antigens. For the B/Beijing/184/93-like antigen, United States manufacturers will use the antigenically equivalent strain B/Harbin/07/94 because of its growth properties.

A summary of the 1997–98 influenza season in Missouri can be found on pages 1–2 of this issue.

Surveys indicate that less than one-half of the high-risk populations receive influenza vaccine each year.** More effective strategies are needed for delivering vaccine to persons at high risk and to their health-care providers and household contacts. Successful vaccination programs have combined education for health-care workers, publicity and education targeted toward potential recipients, a plan for identifying persons at high risk (usually by medical-record review) and efforts to remove administrative and financial barriers that prevent persons from receiving the vaccine.

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* The Morbidity and Mortality Weekly Report (MMWR) is available free of charge in electronic format and on a paid subscription basis for paper copy ($118 per year). To receive an electronic copy on Friday of each week, send an e-mail message to listserv@listserv.cdc.gov. The body content should read SUBscribe mmwr-toc. Electronic copy also is available from CDC's World-Wide Web server at http://www.cdc.gov/epo/mmwr/mmwr.html or from CDC's file transfer protocol server at ftp.cdc.gov/pub/Publications/mmwr. To subscribe for paper copy, contact Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402, Ph: (202) 512-1800.

** In 1996, Medicare provided reimbursement for this vaccine for less than 45.3 percent of its beneficiaries in Missouri. Local health agencies and nursing homes who are not currently Medicare providers may apply, through a simplified application process, for a special provider number which will allow them to receive reimbursement for influenza vaccine given to Medicare beneficiaries. Any questions about this process should be directed to the Section of Vaccine Preventable and Tuberculosis Disease Elimination at (573) 751-6133.

Outpatient Clinics and Physicians' Offices

Staff in physicians' offices, clinics, health-maintenance organizations and employee health clinics should be instructed to identify and label the medical records of patients who should receive vaccine. Vaccine should be offered during visits beginning in September and throughout the influenza season. The offer of vaccine and its receipt or refusal should be documented in the medical record. Patients in high-risk groups who do not have regularly scheduled visits during the fall should be reminded by mail or telephone of the need for vaccine.

Facilities Providing Episodic or Acute Care

Health-care providers in these settings (e.g., emergency rooms and walk-in clinics) should be familiar with influenza vaccine recommendations. They should offer vaccine to persons in high-risk groups or should provide written information on why, where and how to obtain the vaccine.

Nursing Homes and Other Residential Long-Term-Care Facilities

Vaccination should be routinely provided to all residents of chronic-care facilities with the concurrence of attending physicians rather than by obtaining individual vaccination orders on each patient. Consent for vaccination should be obtained from the resident or a family member at the time of admission to the facility, and all residents should be vaccinated at one time, immediately preceding the influenza season. Residents admitted during the winter months after completion of the vaccination program should be vaccinated when they are admitted.

Acute-Care Hospitals

All persons 65 years of age or older, and younger persons (including children) with high-risk conditions who are hospitalized at any time from September through March, should be offered and strongly encouraged to receive influenza vaccine before they are discharged. Household members and others with whom they will have contact should receive written information about why and where to obtain influenza vaccine.

Visiting Nurses and Others Providing Home Care to Persons at High Risk

Nursing care plans should identify patients in high risk groups, and vaccine should be provided in the home if necessary. Caregivers and other persons in the household (including children) should be referred for vaccination.

Health Care Workers

Administrators of all health-care facilities should arrange for influenza vaccine to be offered to all personnel before the influenza season. Personnel should be provided with appropriate educational materials and strongly encouraged to receive vaccine. Particular emphasis should be placed on vaccination of persons who care for members of high-risk groups (e.g., staff of intensive care units [including newborn intensive care units], staff of medical/surgical units and employees of nursing home and chronic care facilities). Using a mobile cart to take vaccine to hospital wards or other work sites and making vaccine available during night and weekend work shifts can enhance compliance, as can a follow-up campaign early in the course of a community outbreak.

Persons Traveling to Foreign Countries

Persons preparing to travel to the tropics at any time of year or to the Southern Hemisphere from April through September should review their influenza vaccination histories. If they were not vaccinated the previous fall or winter, they should consider influenza vaccination before travel. Persons in high-risk groups should be especially encouraged to receive the most current vaccine. Persons at high risk who received the previous season's vaccine before travel should be revaccinated in the fall or winter with the current vaccine.

LATE BREAKERS

- Dr. Marion Warwick has accepted a dual role as medical consultant for the Division of Environmental Health and Communicable Disease Prevention, as well as the Bureau Chief of the Bureau of Communicable Disease Control. The former bureau chief, Caryl Collier, has accepted the position of Chief of the Office of Communicable Disease Consultation, QA and Training for the division. In this capacity, Caryl will provide technical assistance and consultation for all division disease outbreak responses. Caryl will also coordinate post-event input and analysis by staff and our partners to enable us to continually improve our response capabilities.

- The Department of Health has seen an increase in enteroviral meningitis for July–August 1998 compared to the same time period in 1997. Due to a large cluster in the St. Louis metropolitan area, serotyping was done and 60% of the specimens submitted from that area were serotyped as echovirus 30. While aseptic meningitis itself is generally self-limited and usually benign, it normally requires the hospitalization of the patient in order to rule out other causes of meningitis.

- The DOH Home Page has recently gone through some changes. Electronic versions of the *Missouri Epidemiologist* can now be found at **http://www.health.state.mo.us/MoEpi/MoEpi.html**.

Missouri EPIDEMIOLOGIST

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The Managing Editor is H. Denny Donnell, Jr, MD, MPH, State Epidemiologist. Production Manager is Diane C. Rackers. Questions or comments should be directed to (573) 751-6128 or toll free (800) 392-0272.

Alternate forms of this publication for persons with disabilities may be obtained by contacting the Missouri Department of Health, Office of Epidemiology, P.O. Box 570, Jefferson City, MO 65102-0570, Ph: (573) 751-6128. TDD users can access the preceding phone number by calling (800) 735-2966.

VIDEOCONFERENCES

The Section of Vaccine Preventable and Tuberculosis Disease Elimination will sponsor the following Centers for Disease Control and Prevention (CDC) satellite broadcasts:

Preparing for the Next Influenza Pandemic

~~November 20, 1998~~ Tentatively Rescheduled for February 25, 1999

This program will identify the main points in the guidelines for influenza pandemic preparedness and discuss a successful local and state preparedness program. In addition, the participants will have the opportunity to form partnerships and to start a plan of action to prepare emergency response plans for handling an influenza pandemic.

Surveillance of Vaccine-Preventable Diseases

December 3, 1998
11:00 a.m.–2:30 p.m.

This program will provide guidelines for vaccine-preventable disease surveillance, case investigation and outbreak control. Updates for the 1997 Surveillance Manual will be provided for the video conference.

The broadcasts feature question-and-answer sessions in which participants can address questions to the course instructors on toll-free telephone lines. Continuing education credits will be offered for a variety of professions.

For more information about the courses, please contact the immunization representative located in your district health office or the Section of Vaccine Preventable and Tuberculosis Disease Elimination at (800) 699-2313.